

## AMENDMENTS TO THE CLAIMS

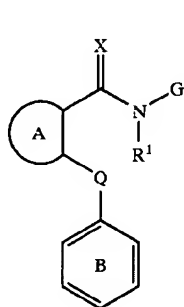
This listing of claims will replace all prior versions, and listing, of claims in the application:

### Listing of Claims:

Please amend the claims as follows:

Claim 1. (Presently amended)

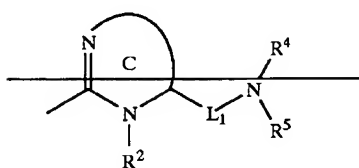
A compound of formula I:



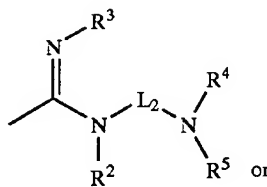
or a pharmaceutically acceptable salt thereof, wherein:

X is oxygen or sulfur;

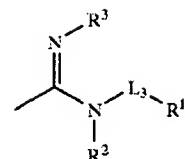
G is G1, G2 or G3:



G1



G2



G3

~~Ring C of G1 is an optionally substituted 5-6 membered aromatic or non-aromatic ring having two or three ring nitrogens;~~

~~L1 is a C<sub>1-6</sub> alkylidene chain optionally substituted by 1-3 R<sup>6</sup>, wherein the alkylidene chain is optionally interrupted by -C(R<sup>11</sup>)<sub>2</sub>-, -C(R<sup>11</sup>)<sub>2</sub>C(R<sup>11</sup>)<sub>2</sub>-, -C(R<sup>11</sup>)=C(R<sup>11</sup>)-, -C≡C-, -O-, -S-, N(R<sup>1</sup>), N(R<sup>10</sup>)CO-, N(R<sup>11</sup>)CO<sub>2</sub>-, CON(R<sup>10</sup>)-, C(R<sup>11</sup>)(OR<sup>1</sup>), CO-, CO<sub>2</sub>-, -OC(-O)-, OC(-O)N(R<sup>10</sup>)-, SO-, SO<sub>2</sub>-, N(R<sup>10</sup>)SO<sub>2</sub>-, or SO<sub>2</sub>N(R<sup>10</sup>)-, and wherein L1 or a portion thereof optionally forms part of a 3-7 membered ring;~~

~~L2 is a C<sub>2-6</sub> alkylidene chain optionally substituted by 1-3 R<sup>6</sup>, wherein the alkylidene chain is optionally interrupted by -C(R<sup>11</sup>)<sub>2</sub>-, -C(R<sup>11</sup>)<sub>2</sub>C(R<sup>11</sup>)<sub>2</sub>-, -C(R<sup>11</sup>)=C(R<sup>11</sup>)-, -C≡C-, -O-,~~

$-\text{S}-$ ,  $-\text{N}(\text{R}^{11})_2-$ ,  $-\text{N}(\text{R}^{10})\text{CO}-$ ,  $-\text{N}(\text{R}^{10})\text{CO}_2-$ ,  $-\text{CON}(\text{R}^{10})-$ ,  $-\text{C}(\text{R}^{11})(\text{OR}^1)-$ ,  $-\text{CO}-$ ,  $-\text{CO}_2-$ ,  $-\text{OC}(=\text{O})-$ ,  $-\text{OC}(=\text{O})\text{N}(\text{R}^{10})-$ ,  $-\text{SO}-$ ,  $-\text{SO}_2-$ ,  $-\text{N}(\text{R}^{10})\text{SO}_2-$  or  $-\text{SO}_2\text{N}(\text{R}^{10})-$ , and wherein  $\text{L}_2$  or a portion thereof optionally forms part of a 3-7 membered ring;

$\text{L}_3$  is a direct link, a  $\text{C}_{0-6}$  alkylidene chain optionally substituted by 1-3  $\text{R}^6$ , wherein the alkylidene chain is optionally interrupted by  $-\text{C}(\text{R}^{11})_2-$ ,  $-\text{C}(\text{R}^{11})_2\text{C}(\text{R}^{11})_2-$ ,  $-\text{C}(\text{R}^{11})=\text{C}(\text{R}^{11})-$ ,  $-\text{C}\equiv\text{C}-$ ,  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{N}(\text{R}^{11})$ ,  $-\text{N}(\text{R}^{10})\text{CO}-$ ,  $-\text{N}(\text{R}^{10})\text{CO}_2-$ ,  $-\text{CON}(\text{R}^{10})-$ ,  $-\text{C}(\text{R}^{11})(\text{OR}^1)-$ ,  $-\text{CO}-$ ,  $-\text{CO}_2-$ ,  $-\text{OC}(=\text{O})-$ ,  $-\text{OC}(=\text{O})\text{N}(\text{R}^{10})-$ ,  $-\text{SO}-$ ,  $-\text{SO}_2-$ ,  $-\text{N}(\text{R}^{10})\text{SO}_2-$ , or  $-\text{SO}_2\text{N}(\text{R}^{10})-$ , and wherein  $\text{L}_3$  or a portion thereof optionally forms part of a 3-7 membered ring;

$\text{R}^1$  is hydrogen or  $\text{C}_{1-6}$  aliphatic;

each  $\text{R}^2$  is independently selected from hydrogen,  $\text{C}_{1-8}$  aliphatic,  $\text{C}_{6-10}$  aryl,  $\text{C}_{7-10}$  aralkyl, or, when Ring C is a 6-membered aromatic ring  $\text{R}^2$  is a lone electron pair;

$\text{R}^3$  is hydrogen,  $\text{C}_{1-8}$  aliphatic,  $\text{C}_{6-10}$  aryl, or  $\text{C}_{7-10}$  aralkyl;

$\text{R}^4$  is hydrogen,  $\text{C}_{1-8}$  aliphatic,  $\text{C}=\text{O}(\text{C}_{1-8}$  aliphatic),  $\text{CO}_2(\text{C}_{1-8}$  aliphatic),  $\text{C}(=\text{O})\text{N}(\text{R}^{10})(\text{C}_{1-7}$  aliphatic),  $\text{C}_{6-10}$  aryl, heteroaryl,  $\text{C}_{7-12}$  aralkyl, or heteroaralkyl;

$\text{R}^5$  is hydrogen or  $\text{C}_{1-8}$  aliphatic, or  $\text{R}^4$  and  $\text{R}^5$  taken together with their intervening nitrogen form a substituted or unsubstituted, aromatic or non-aromatic, 4-14 membered monocyclic, bicyclic or tricyclic ring system having, in addition to said intervening nitrogen, 0-4 ring heteroatoms selected from nitrogen, sulfur or oxygen;

Ring A is a 5-membered heteroaryl ring or a 6-membered aromatic ring having 0-2 ring nitrogen atoms, wherein Q and  $\text{C}(=\text{X})\text{N}(\text{R}^1)-\text{G}$  are attached at ortho positions on Ring A and wherein Ring A is optionally substituted by one to three  $\text{R}^7$ ;

Ring B is a 6-membered aromatic ring having 0-2 ring nitrogen atoms, wherein Ring B is optionally substituted by one or more  $\text{R}^8$ ;

Q is a  $\text{C}_2-\text{C}_4$  alkylidene chain optionally substituted by one to three  $\text{R}^9$ , wherein a methylene unit of the alkylidene chain is optionally replaced by  $-\text{S}-$ ,  $-\text{S}(\text{O})-$ ,  $-\text{SO}_2-$ ,  $-\text{N}(\text{R}^1)-$ ,  $-\text{O}-$ ,  $-\text{C}(\text{O})-$ , or  $-\text{C}(\text{S})-$ ;

each  $\text{R}^6$  is independently selected from halo,  $-\text{OR}^1$ ,  $-\text{CN}$ ,  $-\text{C}_{1-6}$  aliphatic,  $-\text{N}(\text{R}^{10})_2$ ,  $-\text{C}=\text{O}(\text{C}_{1-5}$  aliphatic),  $-\text{CO}_2\text{R}^1$ ,  $-\text{CH}_2\text{CO}_2\text{R}^1$ , or  $-\text{C}(=\text{O})\text{N}(\text{R}^{10})(\text{C}_{1-5}$  aliphatic);

each  $\text{R}^7$  is independently selected from -halo,  $-\text{NO}_2$ ,  $-\text{CN}$ , or a substituted or unsubstituted group selected from  $-\text{R}^{12}$ ,  $-\text{OR}^1$ ,  $-\text{SR}^{12}$ ,  $-\text{C}_{6-10}$  aryl, -heterocyclyl, -heteroaryl,

-C<sub>6-10</sub> aryl)alkyl, -(heterocyclyl)alkyl, -(heteroaryl)alkyl, -N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>C(O)R<sup>1</sup>,  
-NR<sup>10</sup>C(O)N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>CO<sub>2</sub>R<sup>12</sup>, -CO<sub>2</sub>R<sup>1</sup>, -C(O)R<sup>1</sup>, C(O)N(R<sup>10</sup>)<sub>2</sub>, -OC(O)N(R<sup>10</sup>)<sub>2</sub>,  
-S(O)<sub>2</sub>R<sup>12</sup>, -SO<sub>2</sub>N(R<sup>10</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>12</sup>, -NR<sup>10</sup>SO<sub>2</sub>N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>SO<sub>2</sub>R<sup>12</sup>, or  
-C(=NH)-N(R<sup>10</sup>)<sub>2</sub> or two adjacent R<sup>7</sup> taken together with their intervening atoms form a  
5-6 membered unsaturated or partially unsaturated ring having 0-2 ring heteroatoms  
selected from nitrogen, oxygen or sulfur;

each R<sup>8</sup> is independently selected from -halo, -NO<sub>2</sub>, -CN, or a substituted or unsubstituted  
group selected from -R<sup>12</sup>, -OR<sup>1</sup>, -SR<sup>12</sup>, -C<sub>6-10</sub> aryl, -heterocyclyl, -heteroaryl,  
-C<sub>6-10</sub> aryl)alkyl, -(heterocyclyl)alkyl, -(heteroaryl)alkyl, -N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>C(O)R<sup>1</sup>,  
-NR<sup>10</sup>C(O)N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>CO<sub>2</sub>R<sup>12</sup>, -CO<sub>2</sub>R<sup>1</sup>, -C(O)R<sup>1</sup>, -C(O)N(R<sup>10</sup>)<sub>2</sub>,  
-OC(O)N(R<sup>10</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>12</sup>, -SO<sub>2</sub>N(R<sup>10</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>12</sup>, -NR<sup>10</sup>SO<sub>2</sub>N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>SO<sub>2</sub>R<sup>12</sup>, or  
-C(=NH)-N(R<sup>10</sup>)<sub>2</sub>, or two adjacent R<sup>8</sup> taken together with their intervening atoms form a  
5-6 membered unsaturated or partially unsaturated ring having 0-2 ring heteroatoms  
selected from nitrogen, oxygen or sulfur;

each R<sup>9</sup> is independently selected from halo, OR<sup>1</sup>, CN, C<sub>1-6</sub> aliphatic, N(R<sup>10</sup>)<sub>2</sub>,  
-C=O(C<sub>1-5</sub> aliphatic), CO<sub>2</sub>(C<sub>1-5</sub> aliphatic), or C(=O)N(R<sup>10</sup>)(C<sub>1-5</sub> aliphatic), or R<sup>9</sup> and an  
R<sup>7</sup>, at a position ortho to Q, are taken together with their intervening atoms form a 5-7  
membered unsaturated or partially unsaturated ring having 0-2 ring heteroatoms selected  
from N, O or S;

each R<sup>10</sup> is independently selected from hydrogen, a substituted or unsubstituted C<sub>1-8</sub>  
aliphatic group, C(=O)R<sup>1</sup>, CO<sub>2</sub>R<sup>1</sup>, SO<sub>2</sub>R<sup>1</sup>, or two R<sup>10</sup> on the same nitrogen taken together  
with the nitrogen form a 5-8 membered aromatic or non-aromatic ring having, in addition  
to the nitrogen, 0-2 ring heteroatoms selected from N, O, or S;

each R<sup>11</sup> is independently selected from hydrogen, CO<sub>2</sub>R<sup>12</sup>, CON(R<sup>12</sup>)<sub>2</sub>, OR<sup>12</sup>, or a  
substituted or unsubstituted C<sub>1-8</sub> aliphatic group;

each R<sup>12</sup> is independently selected from a substituted or unsubstituted C<sub>1-8</sub> aliphatic group;

and R<sup>14</sup> is hydrogen, C<sub>1-8</sub> aliphatic, C<sub>6-10</sub> aryl, heteroaryl, C<sub>7-12</sub> aralkyl, heteroaralkyl,  
heterocyclyl, or R<sup>3</sup> and R<sup>14</sup> taken together with their intervening nitrogens form a  
substituted or unsubstituted, aromatic or non-aromatic, 4-14 membered monocyclic,  
bicyclic or tricyclic ring system having, in addition to said intervening nitrogen, 0-4 ring  
heteroatoms selected from nitrogen, sulfur or oxygen;

with the proviso that  $L_3-R^{14}$ , taken together is not H.

Claims 2-6 (Canceled)

Claim 7. (Original) The compound of claim 1 wherein G is G2.

Claim 8. (Original) The compound of claim 7 having one or more features selected from the group consisting of:

- (a) X is oxygen;
- (b)  $L_2$  is a  $C_{3-4}$  alkylidene chain;
- (c) Q is  $-CH_2CH_2-$ ;
- (d) (i)  $R^4$  and  $R^5$  are each independently selected from a  $C_{1-4}$  aliphatic group, or (ii)  $R^4$  And  $R^5$  taken together with their intervening nitrogen form a 5-6 membered ring, or (iii)  $R^5$  is a  $C_{1-4}$  aliphatic group and  $R^4$  is aryl, aralkyl, heteroaryl, or heteroaralkyl;
- (e) Ring A is an optionally substituted phenyl or thienyl; and
- (f) Ring B is a substituted phenyl or naphthyl.

Claim 9. (Original) The compound of claim 7 wherein:

- (a) X is oxygen;
- (b)  $L_2$  is a  $C_{3-4}$  alkylidene chain;
- (c) Q is  $-CH_2CH_2-$ ;
- (d) (i)  $R^4$  and  $R^5$  are each independently selected from a  $C_{1-4}$  aliphatic group, or (ii)  $R^4$  and  $R^5$  taken together with their intervening nitrogen form a 5-6 membered ring, or (iii)  $R^5$  is a  $C_{1-4}$  aliphatic group and  $R^4$  is aryl, aralkyl, heteroaryl, or heteroaralkyl;
- (e) Ring A is phenyl or thienyl; and
- (f) Ring B is phenyl or naphthyl.

Claim 10. (Original) The compound of claim 7 having one or more features selected from the group consisting of:

- (a) X is oxygen;
- (b)  $L_2$  is  $-CH_2CH_2CH_2-$  or  $-CH(CH_3)CH_2CH_2-$ ;

- (c) Q is  $-\text{CH}_2\text{CH}_2-$ ;
- (d)  $\text{R}^4$  and  $\text{R}^5$  are each independently selected from a  $\text{C}_{1-3}$  aliphatic group or  $\text{R}^4$  and  $\text{R}^5$  taken together with their intervening nitrogen form a piperidinyl, pyrrolidinyl, piperazinyl or morpholinyl ring;
- (e) Ring A is an optionally substituted phenyl or thienyl; and
- (f) Ring B is a substituted phenyl or naphthyl.

Claim 11. (Original) The compound of claim 7 wherein:

- (a) X is oxygen;
- (b)  $\text{L}_2$  is  $-\text{CH}_2\text{CH}_2\text{CH}_2-$  or  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$ ;
- (c) Q is  $-\text{CH}_2\text{CH}_2-$ ;
- (d)  $\text{R}^4$  and  $\text{R}^5$  are each independently selected from a  $\text{C}_{1-3}$  aliphatic group or  $\text{R}^4$  and  $\text{R}^5$  taken together with their intervening nitrogen form a piperidinyl, pyrrolidinyl, piperazinyl or morpholinyl ring;
- (e) Ring A is an optionally substituted phenyl or thienyl; and
- (f) Ring B is a substituted phenyl or naphthyl.

Claim 12. (Original) The compound of claim 1 wherein G is G3.

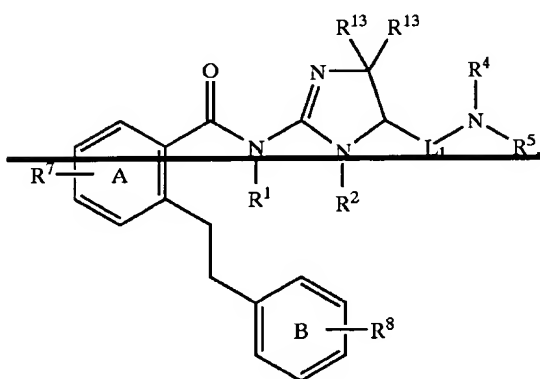
Claim 13. (Original) The compound of claim 12 having one or more features selected from the group consisting of:

- (a) X is oxygen;
- (b)  $\text{L}_3$  is selected from a direct link,  $-\text{CH}_2-$ ,  $-\text{CH}(\text{R}^6)-$ ,  $-\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$ ;
- (c) Q is  $-\text{CH}_2\text{CH}_2-$ ;
- (d)  $\text{R}^5$  is  $\text{C}_{1-3}$  alkyl,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2(\text{C}_{1-6}\text{alkyl})$ ,  $\text{CH}_2\text{CO}_2\text{H}$ , or  $\text{CH}_2\text{CO}_2(\text{C}_{1-6}\text{ alkyl})$ ;
- (e)  $\text{R}^{14}$  is selected from a  $\text{C}_{1-6}$  aliphatic group or a 5-6 membered heterocyclic ring;
- (f) Ring A is an optionally substituted phenyl or thienyl; and
- (g) Ring B is a substituted phenyl or naphthyl.

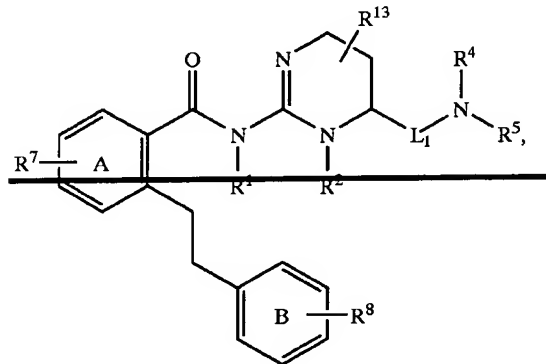
Claim 14. (Original) The compound of claim 12 having one or more features selected from the group consisting of:

- (a) X is oxygen;
- (b) L<sub>3</sub> is -CH<sub>2</sub>- or -CH(R<sup>6</sup>)-;
- (c) R<sup>6</sup> is C<sub>1-3</sub> alkyl, CO<sub>2</sub>H, CO<sub>2</sub>(C<sub>1-6</sub> alkyl), CH<sub>2</sub>CO<sub>2</sub>H, or CH<sub>2</sub>CO<sub>2</sub>(C<sub>1-6</sub> alkyl);
- (d) R<sup>14</sup> is a 5-6 membered heterocyclic ring having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;
- (e) Q is -CH<sub>2</sub>CH<sub>2</sub>-;
- (f) Ring A is an optionally substituted phenyl or thienyl; and
- (g) Ring B is a substituted phenyl or naphthyl.

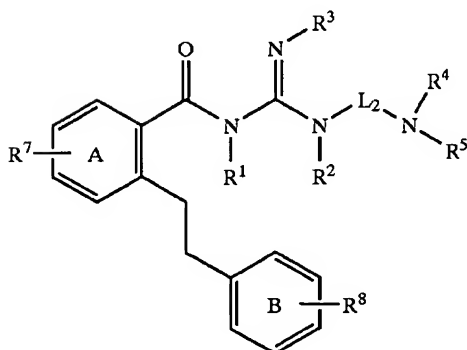
Claim 15. (Presently amended) The compound of claim 1 represented by formulae ~~II-A~~, ~~II-B~~, II-C or II-D:



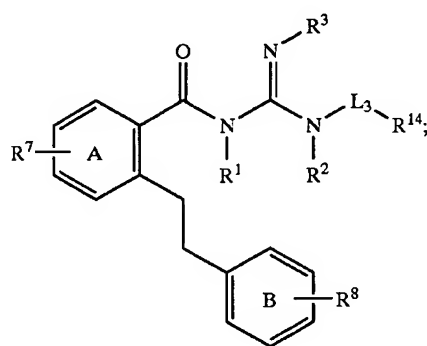
II-A



II-B



II-C



II-D

or

wherein:

$R^1$  and  $R^2$  are each hydrogen;

$R^3$  is hydrogen;

$L_1$  is  $-\text{CH}_2\text{CH}_2-$  or  $-\text{CH}_2\text{CH}_2\text{CH}_2-$ ;

$L_2$  is  $-\text{CH}_2\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$ , or  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2-$ ;

$L_3$  is a direct link,  $-\text{CH}_2-$ ,  $-\text{CH}(\text{R}^6)-$ ,  $-\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{CH}_2-$ , or  $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$ ;

$\text{R}^6$  is  $\text{C}_{1-3}$  alkyl,  $\text{CO}_2\text{H}$ ,  $\text{CO}_2(\text{C}_{1-6}$  alkyl),  $\text{CH}_2\text{CO}_2\text{H}$ , or  $\text{CH}_2\text{CO}_2(\text{C}_{1-6}$  alkyl);

$\text{R}^7$  is absent or is -halo,  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{R}^{12}$ ,  $-\text{OR}^1$ ,  $-\text{SR}^{12}$ ,  $-\text{C}_{6-10}$  aryl, -heterocyclyl, -heteroaryl,  $-(\text{C}_{6-10}$  aryl)alkyl, -(heterocyclyl)alkyl, -(heteroaryl)alkyl,  $-\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{C}(\text{O})\text{R}^1$ ,  $-\text{NR}^{10}\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{CO}_2\text{R}^{12}$ ,  $-\text{CO}_2\text{R}^1$ ,  $-\text{C}(\text{O})\text{R}^1$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{OC}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{S}(\text{O})_2\text{R}^{12}$ ,  $-\text{SO}_2\text{N}(\text{R}^{10})_2$ ,  $-\text{S}(\text{O})\text{R}^{12}$ ,  $-\text{NR}^{10}\text{SO}_2\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{SO}_2\text{R}^{12}$ , or  $-\text{C}(=\text{NH})-\text{N}(\text{R}^{10})_2$ , or two adjacent  $\text{R}^7$  taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

$\text{R}^8$  is -halo,  $-\text{NO}_2$ ,  $-\text{CN}$ , or a substituted or unsubstituted group selected from  $-\text{R}^{12}$ ,  $-\text{OR}^1$ ,  $-\text{SR}^{12}$ ,  $-\text{C}_{6-10}$  aryl, -heterocyclyl, -heteroaryl,  $-(\text{C}_{6-10}$  aryl)alkyl, -(heterocyclyl)alkyl, -heteroaryl)alkyl,  $-\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{C}(\text{O})\text{R}^1$ ,  $-\text{NR}^{10}\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{CO}_2\text{R}^{12}$ ,  $-\text{CO}_2\text{R}^1$ ,  $-\text{C}(\text{O})\text{R}^1$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{OC}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{S}(\text{O})_2\text{R}^{12}$ ,  $-\text{SO}_2\text{N}(\text{R}^{10})$ .sub- .2,  $-\text{S}(\text{O})\text{R}^{12}$ ,  $-\text{NR}^{10}\text{SO}_2\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{SO}_2\text{R}^{12}$ , or  $-\text{C}(=\text{NH})-\text{N}(\text{R}^{10})_2$ , or two adjacent  $\text{R}^8$  taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

$\text{R}^4$  and  $\text{R}^5$  (i) are each independently selected from a  $\text{C}_{1-4}$  aliphatic group, or (ii)  $\text{R}^4$  and  $\text{R}^5$  taken together with their intervening nitrogen form a 5-6 membered ring, or (iii)  $\text{R}^4$  is a  $\text{C}_{1-4}$  aliphatic group and  $\text{R}^5$  is aryl, aralkyl, heteroaryl, or heteroaralkyl;

$\text{R}^{14}$  is a  $\text{C}_{1-6}$  aliphatic or 5-6 membered heterocyclic ring or  $\text{R}^{13}$  and  $\text{R}^{14}$  taken together with their intervening nitrogens form a 4-6 membered ring;

~~each  $\text{R}^{13}$  is independently selected from hydrogen,  $\text{C}_{1-6}$  aliphatic, or a substituent selected from the group consisting of  $\text{COR}^1$ ,  $\text{CO}_2\text{R}^1$ ,  $\text{CN}$ ,  $-\text{N}(\text{R}^{10})_2$ ,  $-\text{CON}(\text{R}^{10})_2$ ,  $-\text{OR}^1$ , or two  $\text{R}^{13}$  on the same carbon taken together form  $=\text{O}$ , or two  $\text{R}^{13}$  taken together with their intervening atoms form a 3-7 membered ring having 0-2 ring heteroatoms;~~

each  $R^{10}$  is independently selected from hydrogen, a substituted or unsubstituted  $C_{1-8}$  aliphatic group,  $C(=O)R^1$ ,  $CO_2R^1$ ,  $SO_2R^1$ , or two  $R^{10}$  on the same nitrogen taken together with the nitrogen form a 5-8 membered aromatic or non-aromatic ring having, in addition to the nitrogen, 0-2 ring heteroatoms selected from N, O, or S;  
each  $R^{11}$  is independently selected from hydrogen or an optionally substituted  $C_{1-8}$  aliphatic group; and  
each  $R^{12}$  is independently selected from a substituted or unsubstituted  $C_{1-8}$  aliphatic group.

Claim 16. (Presently Amended)      The compound of claim 15 wherein:

$R^1$  and  $R^2$  are each hydrogen;

$R^3$  is hydrogen;

$L_1$  is  $-CH_2CH_2-$  or  $-CH_2CH_2CH_2-$ ;

$L_2$  is  $-CH_2CH_2CH_2-$ ,  $-CH_2CH_2CH_2CH_2-$ ,  $-CH(CH_3)CH_2CH_2-$ , or  $-CH(CH_3)CH_2CH_2CH_2-$ ;

$L_3$  is a direct link,  $-CH_2-$ ,  $-CH(R^6)-$ ,  $-CH_2CH_2-$ ,  $-CH_2CH_2CH_2-$ , or  $-CH_2CH_2CH_2CH_2-$ ;

$R^6$  is  $CO_2H$ ,  $CO_2(C_{1-6} \text{ alkyl})$ ,  $CH_2CO_2H$ , or  $CH_2CO_2(C_{1-6} \text{ alkyl})$ ;

$R^7$  is absent or is -halo,  $-CN$ ,  $-R^{12}$ ,  $-OR^1$ ,  $-SR^{12}$ ,  $-N(R^{10})_2$ ,  $-NR^{10}C(O)R^1$ ,  $-NR^{10}C(O)N(R^{10})_2$ ,  $-NR^{10}CO_2R^{12}$ ,  $-CO_2R^1$ ,  $-C(O)R^1$ ,  $-C(O)N(R^{10})_2$ ,  $-OC(O)N(R^{11})_2$ ,  $-S(O)_2R^{12}$ ,  $-SO_2N(R^{10})_2$ ,  $-S(O)R^{12}$ ,  $-NR^{10}SO_2N(R^{10})_2$ , or  $-NR^{10}SO_2R^{12}$ ;

$R^8$  is -halo,  $-CN$ , or a substituted or unsubstituted group selected from  $-R^{12}$ ,  $-OR^1$ ,  $-SR^{12}$ ,  $-N(R^{10})_2$ ,  $-NR^1$ ,  $-C(O)R^1$ ,  $-NR^{10}CO_2R^{12}$ ,  $-CO_2R^1$ ,  $-C(O)$ ,  $-C(O)N(R^{10})_2$ ,  $-OC(O)N(R^{10})R^{12}$ ,  $-S(R^{10})_2R^{12}$ ,  $-SO_2N(R^{10})_2$ ,  $-S(O)R^{12}$ ,  $-NR^{10}SO_2N(R^{10})_2$ , or  $-NR^{10}SO_2R^{12}$ , or two adjacent  $R^8$  taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

$R^4$  and  $R^5$  are each independently selected from  $C_{1-3}$  alkyl or  $R^4$  and  $R^5$  taken together with their intervening nitrogen form a 5-6 membered ring;

$R^{14}$  is a  $C_{1-6}$  aliphatic or a 5-6 membered heterocyclic ring having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;

each  $R^{13}$  is hydrogen;

each  $R^{10}$  is hydrogen;





III-C

III-D

wherein:

$R^1$ , and  $R^2$  are each hydrogen;

$R^3$  is hydrogen;

$L_1$  is  $-\text{CH}_2\text{CH}_2-$  or  $-\text{CH}_2\text{CH}_2\text{CH}_2-$ ;

$L_2$  is  $-\text{CH}_2\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2-$ ,  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2-$ , or  $-\text{CH}(\text{CH}_3)\text{CH}_2\text{CH}_2\text{CH}_2-$ ;

$L_3$  is a direct link,  $-\text{CH}_2-$ , or  $-\text{CH}_2\text{CH}_2-$ ;

$R^7$  is absent or is -halo,  $-\text{CO}_2R^1$ ,  $-\text{C}(\text{O})R^1$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ , or two adjacent  $R^7$  taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

$R^8$  is -halo,  $-\text{NO}_2$ ,  $-\text{CN}$ , or a substituted or unsubstituted group selected from  $-\text{R}^{12}$ ,  $-\text{OR}^1$ ,  $-\text{SR}^{12}$ ,  $-\text{C}_{6-10}$  aryl, -heterocyclyl, -heteroaryl,  $-(\text{C}_{6-10}$  aryl)alkyl, -(heterocyclyl)alkyl, -heteroaryl)alkyl,  $-\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{C}(\text{O})R^1$ ,  $-\text{NR}^{10}\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{CO}_2R^{12}$ ,  $-\text{CO}_2R^1$ ,  $-\text{C}(\text{O})R^1$ ,  $-\text{C}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{OC}(\text{O})\text{N}(\text{R}^{10})_2$ ,  $-\text{S}(\text{O})_2R^{12}$ ,  $-\text{SO}_2\text{N}(\text{R}^{10})_2$ ,  $-\text{S}(\text{O})R^{12}$ ,  $-\text{NR}^{10}\text{SO}_2\text{N}(\text{R}^{10})_2$ ,  $-\text{NR}^{10}\text{SO}_2R^{12}$ , or  $-\text{C}(=\text{NH})-\text{N}(\text{R}^{10})_2$ , or two adjacent  $R^8$  taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

$R^4$  and  $R^5$  are each independently selected from  $\text{C}_{1-3}$  alkyl or  $R^4$  and  $R^5$  taken together with their intervening nitrogen form a 5-6 membered ring;

$R^{14}$  is a  $\text{C}_{1-6}$  aliphatic or a 5-6 membered heterocyclic ring having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;

~~each  $R^{13}$  is independently selected from hydrogen,  $\text{C}_{1-6}$  aliphatic, or a substituent selected from the group consisting of  $\text{COR}^1$ ,  $\text{CO}_2R^1$ ,  $\text{CN}$ ,  $\text{N}(\text{R}^{10})_2$ ,  $\text{CON}(\text{R}^{10})_2$ ,  $\text{OR}^1$ , or two  $R^{13}$  on the same carbon taken together form  $=\text{O}$ , or two  $R^{13}$  taken together with their intervening atoms form a 3-7 membered ring having 0-2 ring heteroatoms;~~

each  $R^{10}$  is independently selected from hydrogen, a substituted or unsubstituted  $\text{C}_{1-8}$  aliphatic group,  $\text{C}(=\text{O})R^1$ ,  $\text{CO}_2R^1$ ,  $\text{SO}_2R^1$ , or two  $R^{10}$  on the same nitrogen taken together with the nitrogen form a 5-8 membered aromatic or non-aromatic ring having, in addition to the nitrogen, 0-2 ring heteroatoms selected from N, O, or S;

each  $R^{11}$  is independently selected from hydrogen or an optionally substituted  $\text{C}_{1-8}$  aliphatic group;

and each R<sup>12</sup> is independently selected from a substituted or unsubstituted C<sub>1-8</sub> aliphatic group.

Claim 19. (Presently Amended) The compound of claim 18 wherein:

R<sup>1</sup>, R<sup>2</sup>, and R<sup>3</sup> are each hydrogen;

L<sub>1</sub> is -CH<sub>2</sub>CH<sub>2</sub>- or -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-;

L<sub>2</sub> is -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-, -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>-, or -CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>-;

L<sub>3</sub> is a direct link, -CH<sub>2</sub>-, or -CH<sub>2</sub>CH<sub>2</sub>-;

R<sup>7</sup> is absent;

R<sup>8</sup> is -halo, -CN, or a substituted or unsubstituted group selected from -R<sup>12</sup>, -OR<sup>1</sup>, -SR<sup>12</sup>, -N(R<sup>10</sup>)<sub>2</sub>, -NR<sup>10</sup>C(O)R<sup>1</sup>, -NR<sup>10</sup>CO<sub>2</sub>R<sup>12</sup>, -CO<sub>2</sub>R<sup>1</sup>, -C(O)R<sup>1</sup>, -O(O)N(R<sup>10</sup>)<sub>2</sub>, -OC(O)N(R<sup>10</sup>)<sub>2</sub>, -S(O)<sub>2</sub>R<sup>12</sup>, -SO<sub>2</sub>N(R<sup>10</sup>)<sub>2</sub>, -S(O)R<sup>12</sup>, -NR<sup>10</sup>SO<sub>2</sub>N(R<sup>10</sup>)<sub>2</sub>, or -NR<sup>10</sup>SO<sub>2</sub>R<sup>12</sup>, or two adjacent R<sup>8</sup> taken together with their intervening atoms form a 5-6 membered unsaturated or partially unsaturated ring having 0-2 heteroatoms selected from nitrogen, oxygen or sulfur;

R<sup>4</sup> and R<sup>5</sup> are each independently selected from C<sub>1-3</sub> alkyl or R<sup>4</sup> and R<sup>5</sup> taken together with their intervening nitrogen form a 5-6 membered ring;

R<sup>14</sup> is a C<sub>1-6</sub> aliphatic or a 5-6 membered heterocyclic ring having a ring nitrogen and 0-1 additional ring heteroatoms selected from N, O or S;

~~each R<sup>13</sup> is hydrogen;~~

each R<sup>10</sup> is hydrogen;

each R<sup>11</sup> is independently selected from hydrogen or an optionally substituted C<sub>1-5</sub> aliphatic group;

and each R<sup>12</sup> is independently selected from a substituted or unsubstituted C<sub>1-5</sub> aliphatic group.

Claim 20. (Original) The compound of claim 18 wherein:

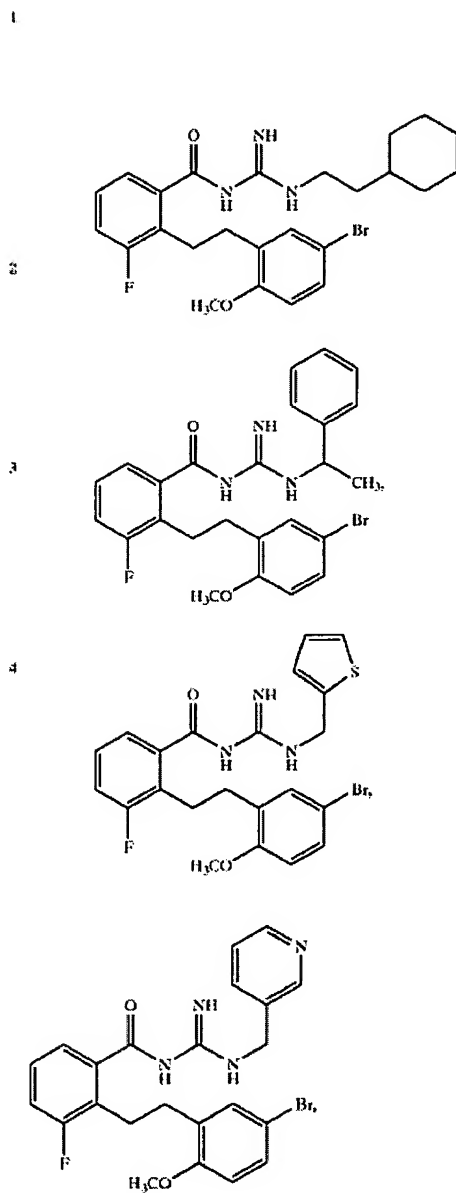
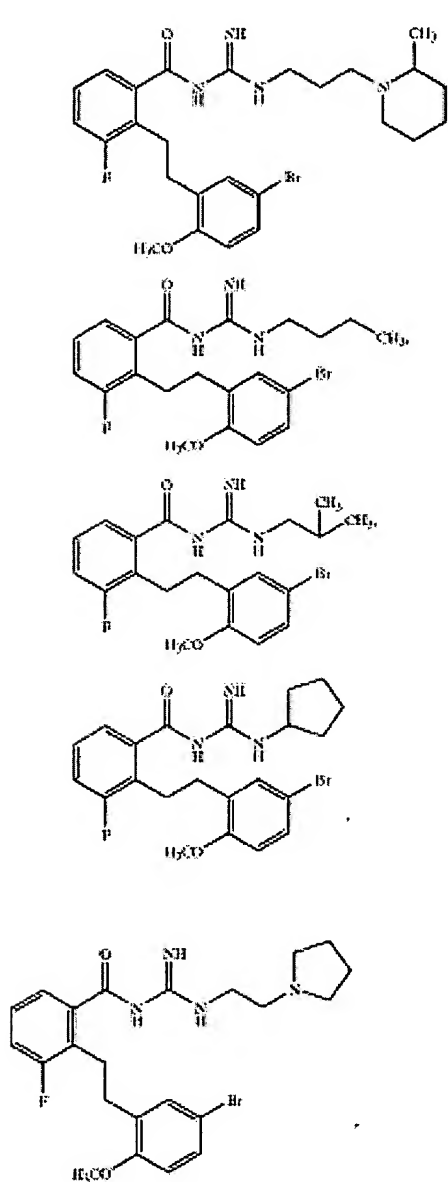
Ring B is a phenyl ring having two R<sup>8</sup> substituents that are para to one another or Ring B is a naphthyl ring;

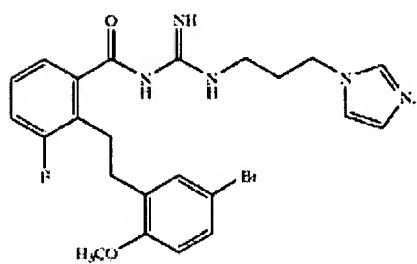
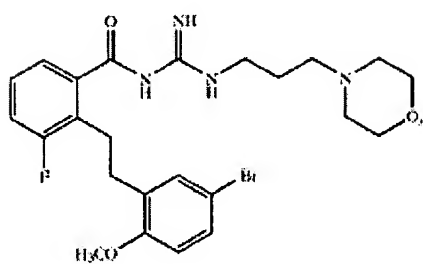
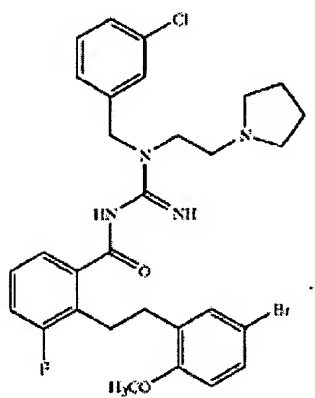
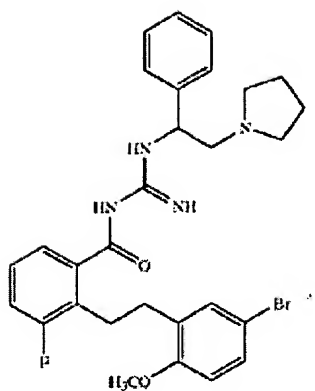
and Each R<sup>8</sup> is independently selected from halo, C<sub>1-4</sub> alkyl, C<sub>1-3</sub> alkoxy, CO(C<sub>1-3</sub> alkyl), CONH(C<sub>1-3</sub> alkyl), SO<sub>2</sub>(C<sub>1-3</sub> alkyl), or SO<sub>2</sub>NH(C<sub>1-3</sub> alkyl).

**Claim 21. (Presently Amended)**

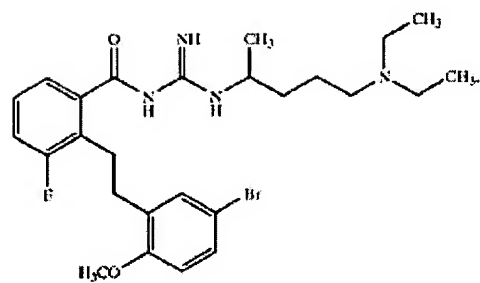
A compound according to claim 1 selected from the

group consisting of:



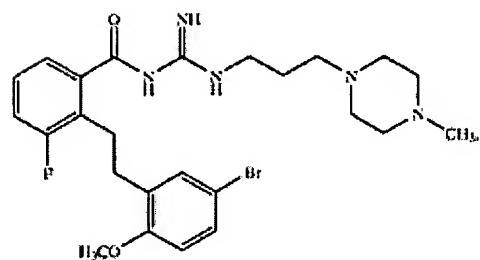


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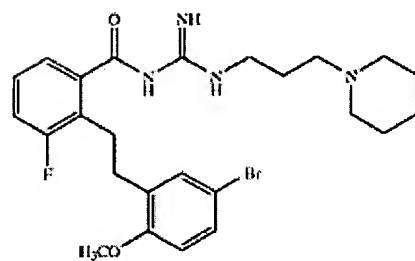
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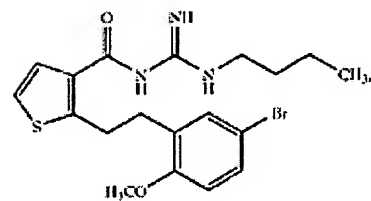
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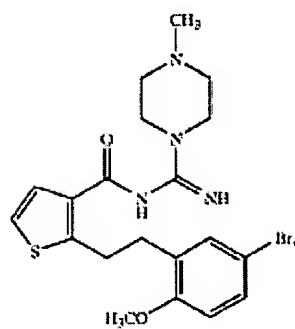
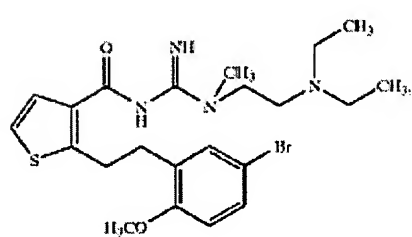
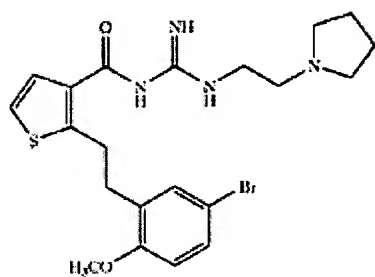
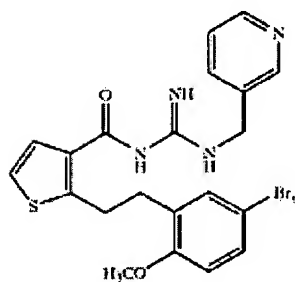
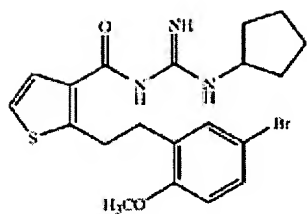


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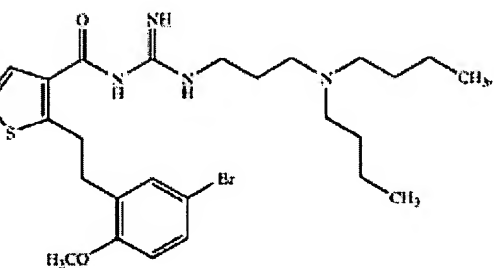
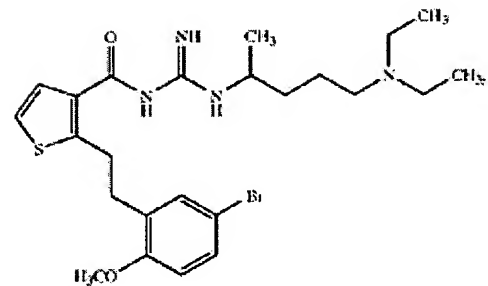
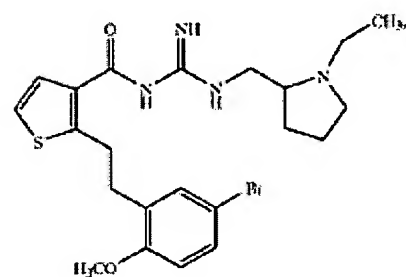
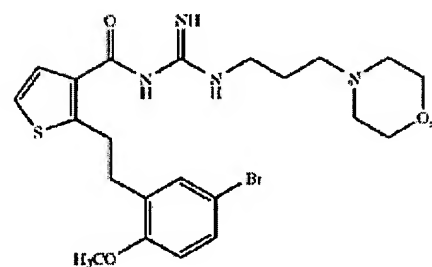
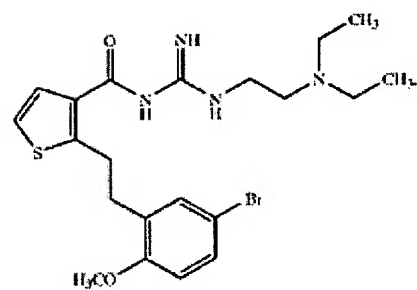
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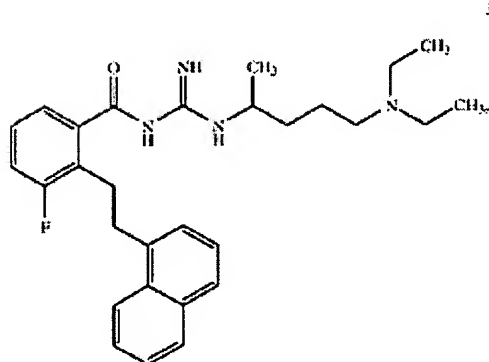
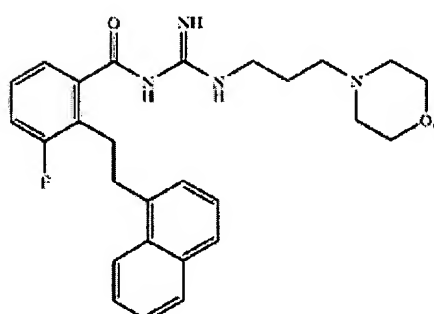
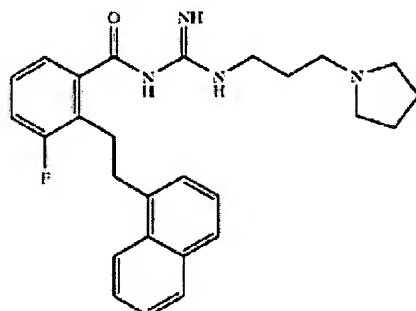
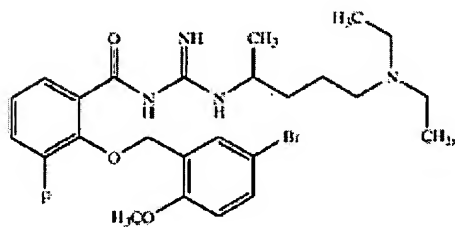
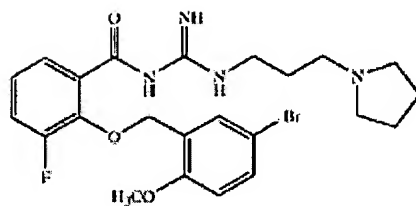
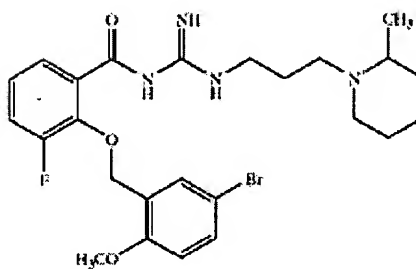
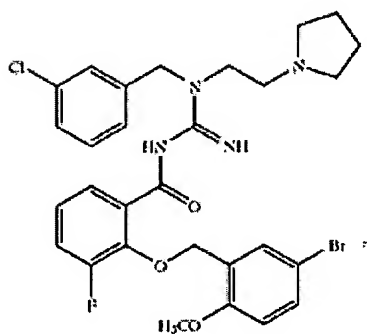
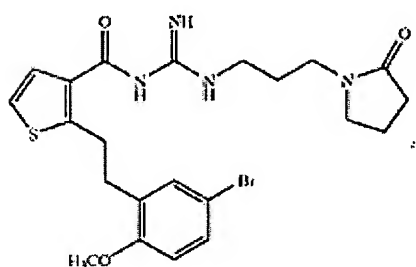
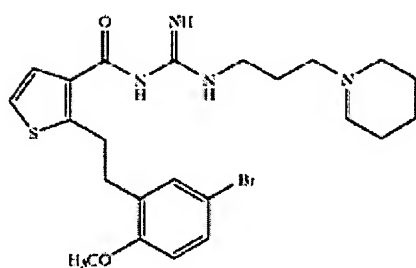
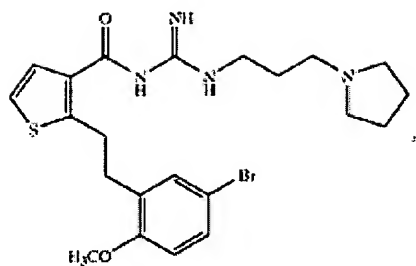
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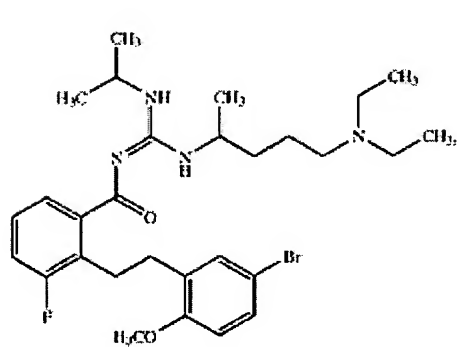
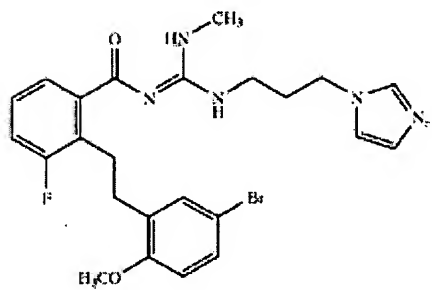
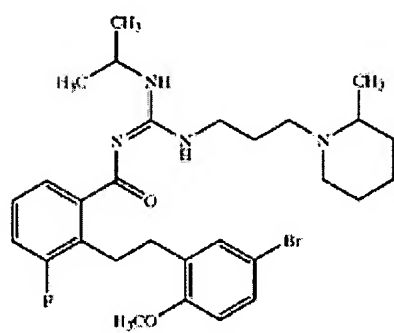
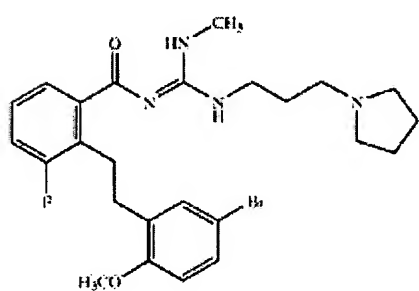
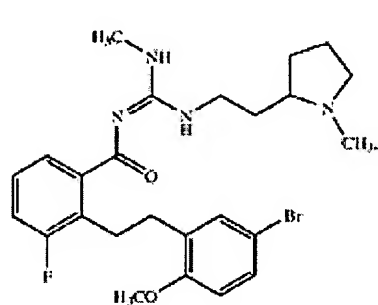
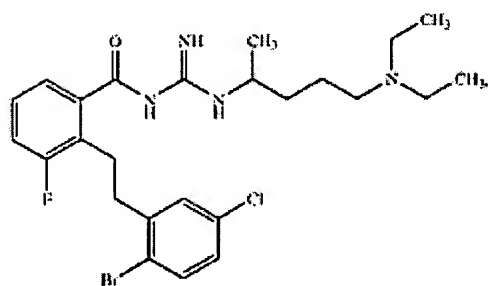
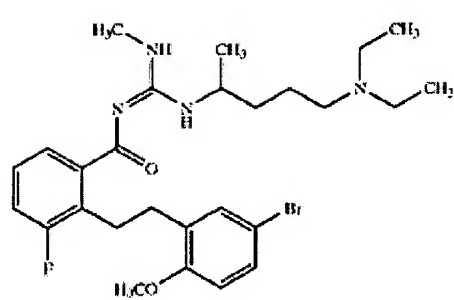
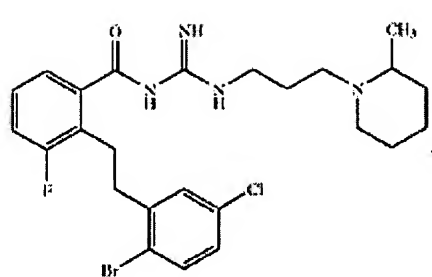
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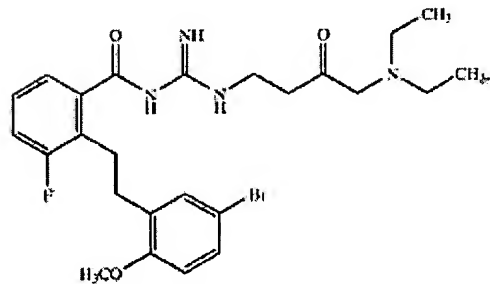
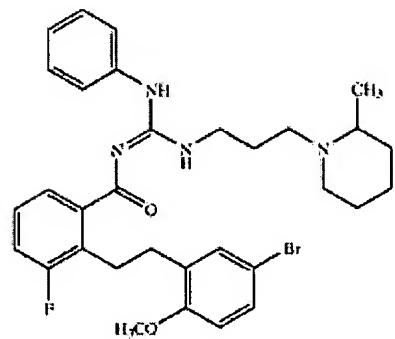
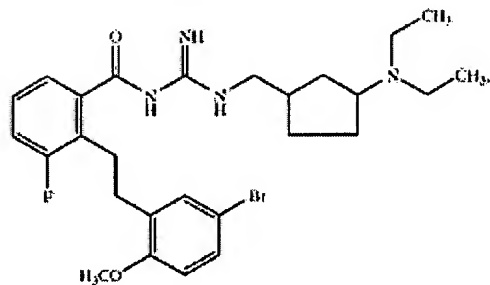
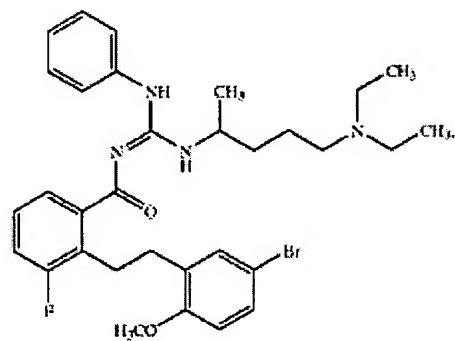
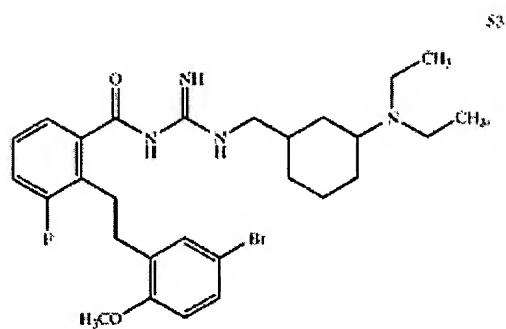
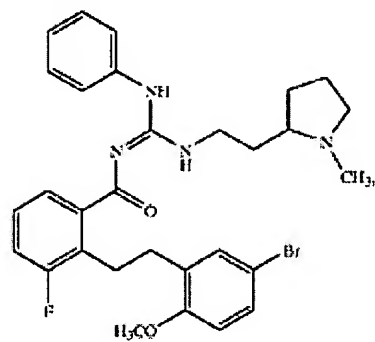
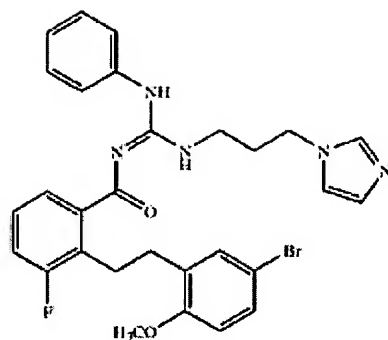
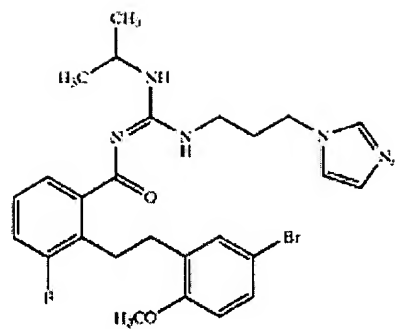
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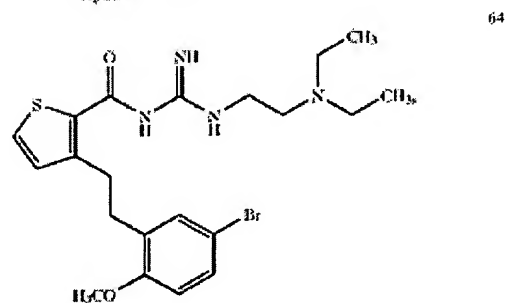
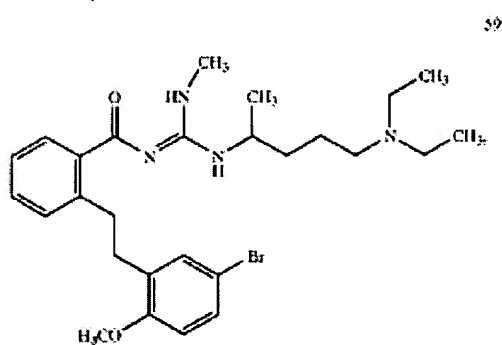
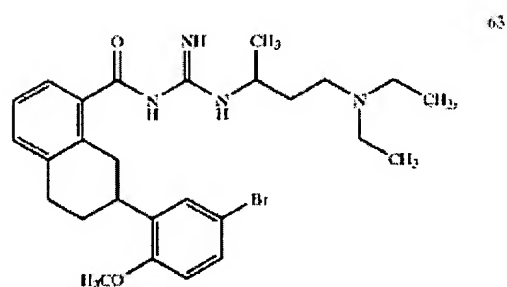
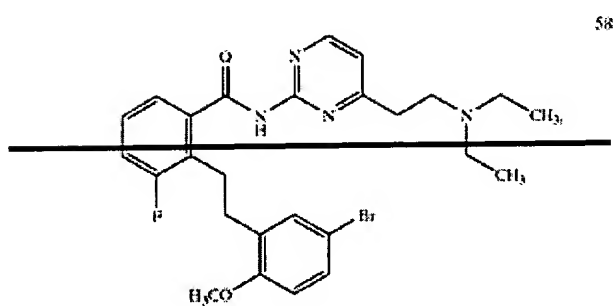
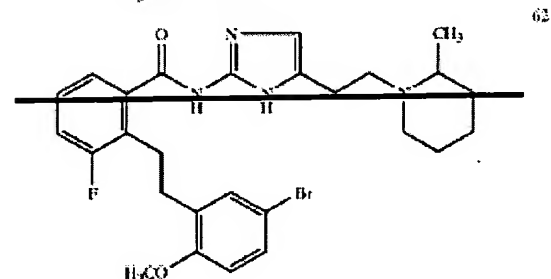
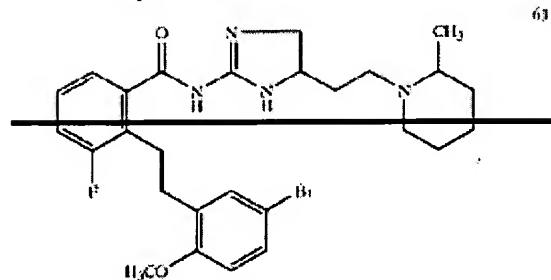
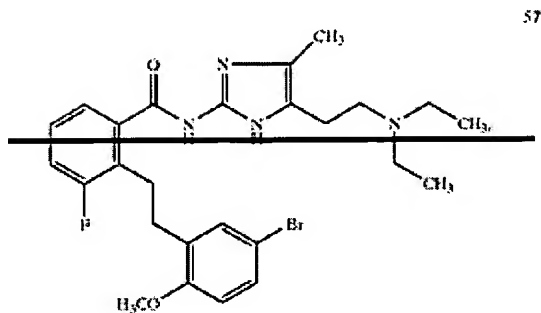
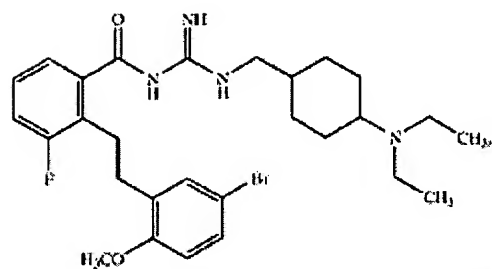
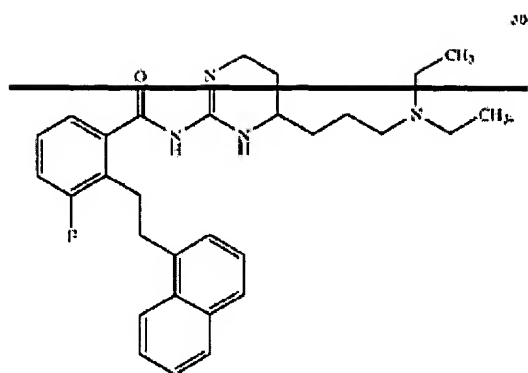
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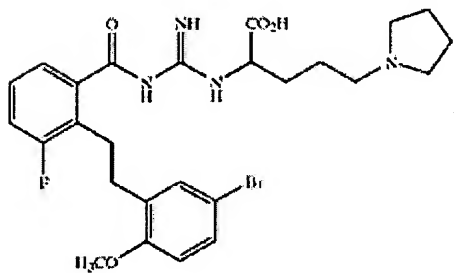
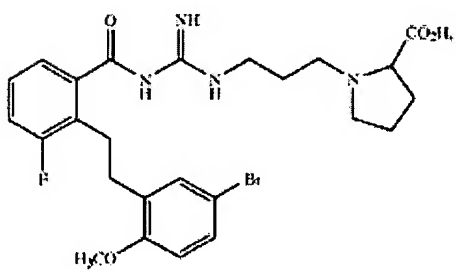
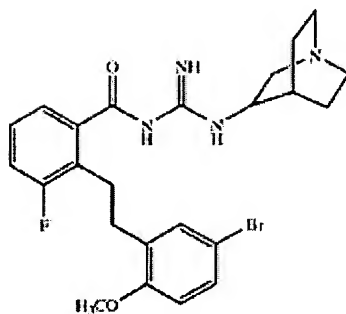
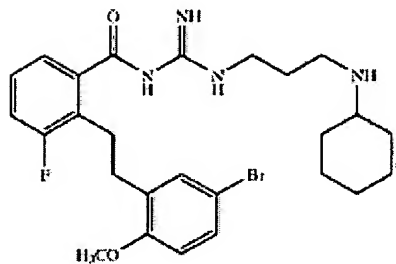
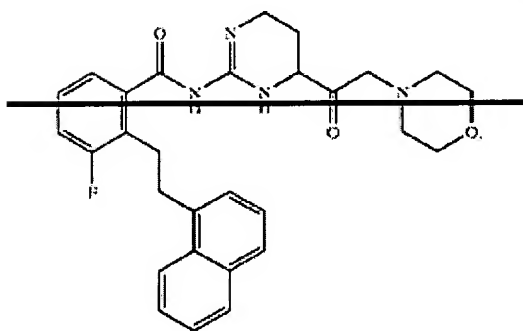
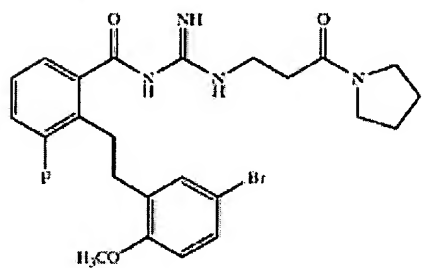
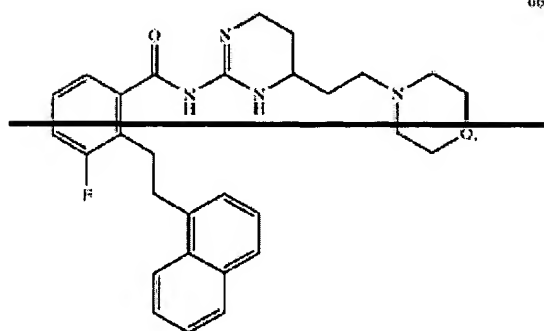
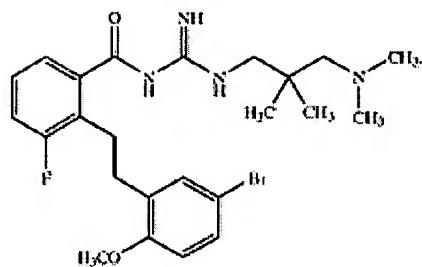
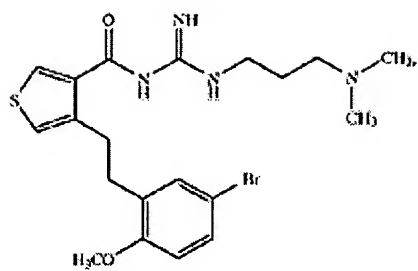


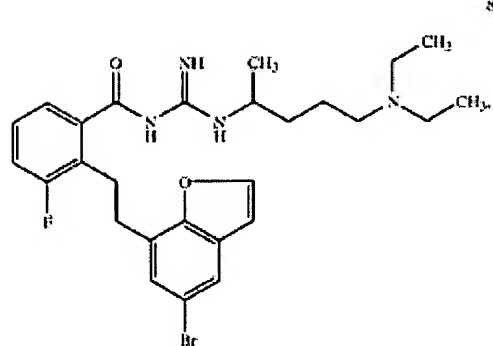
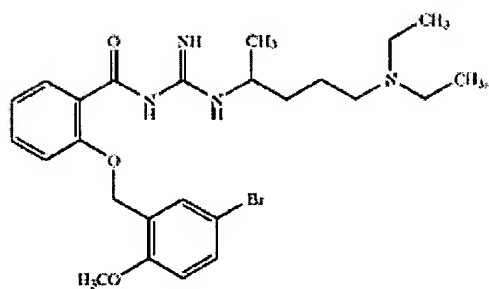
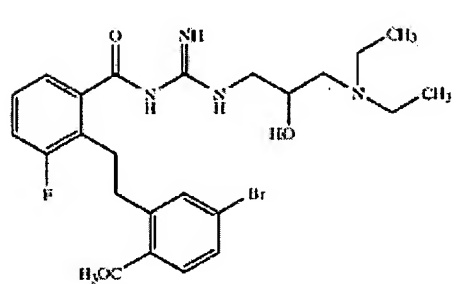
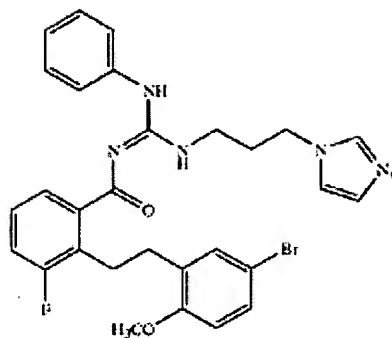
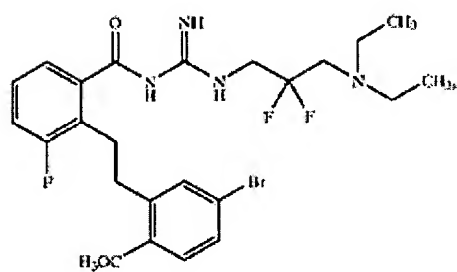
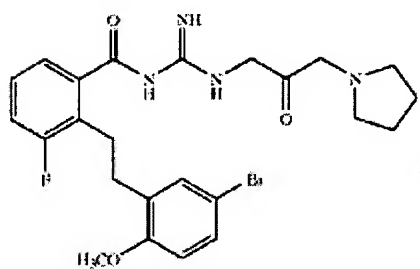
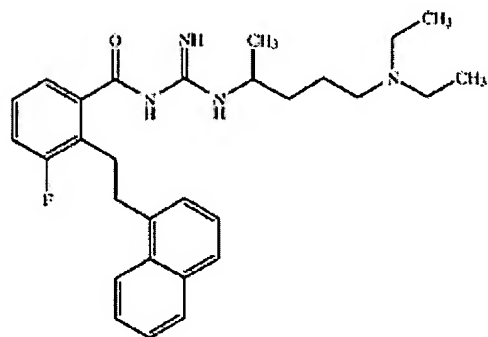
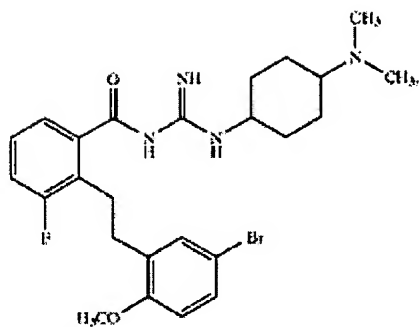


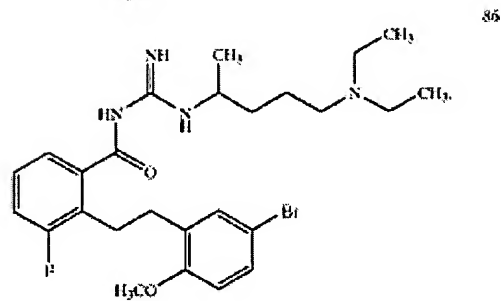
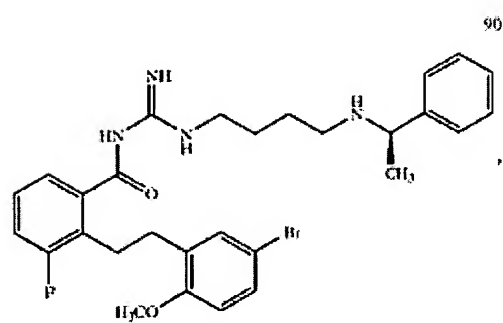
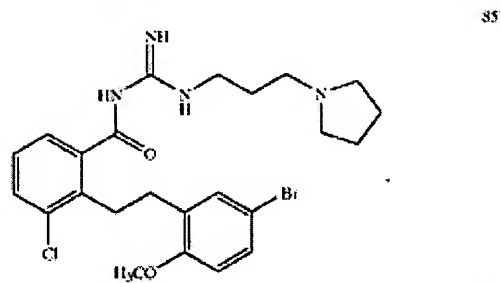
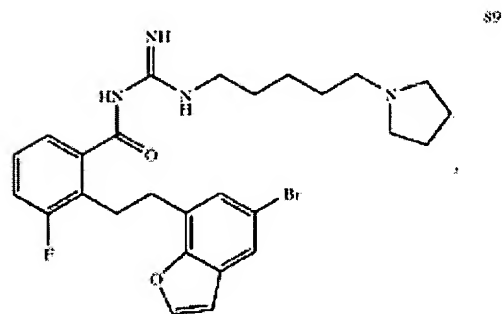
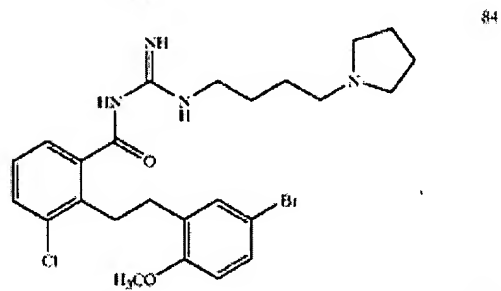
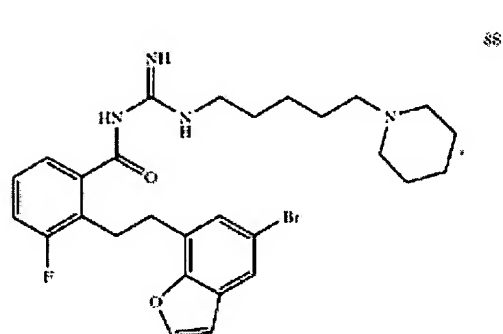
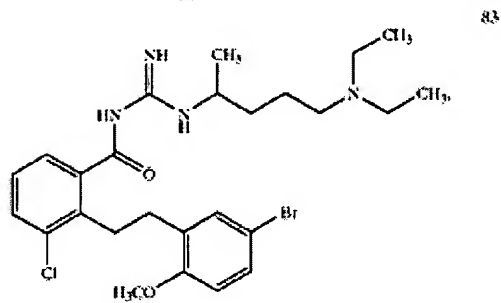
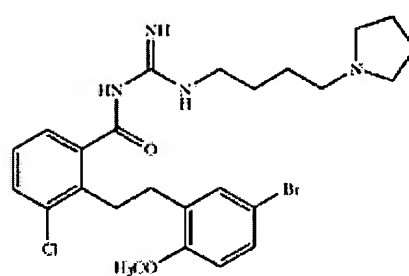
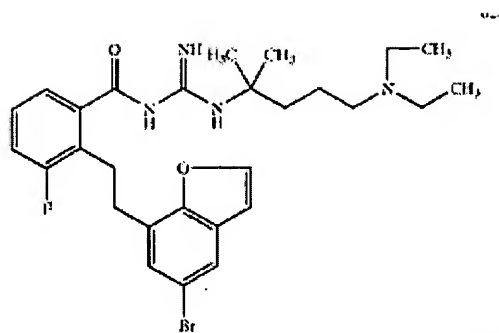


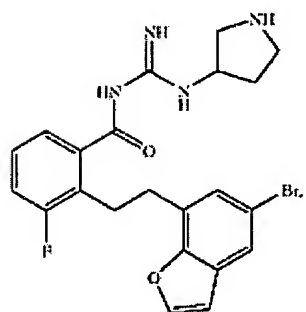
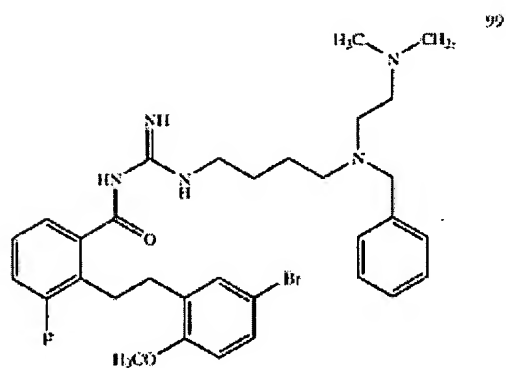
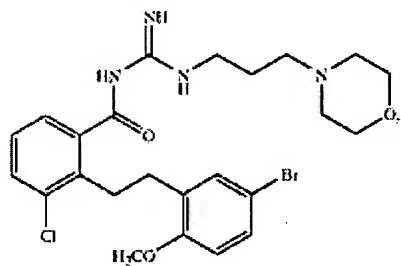
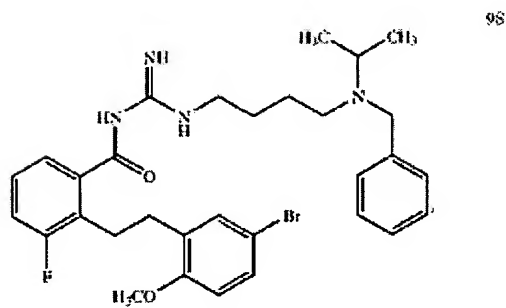
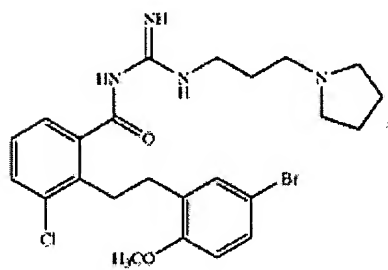
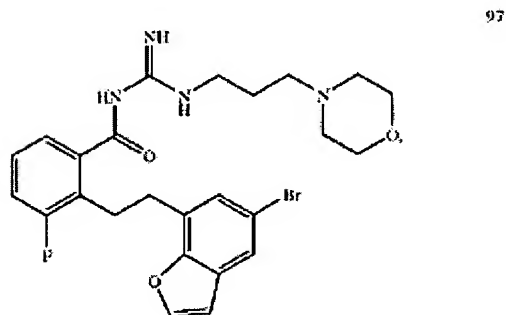
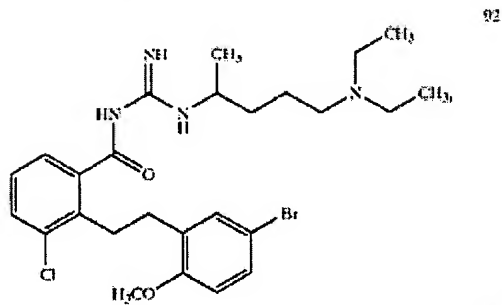
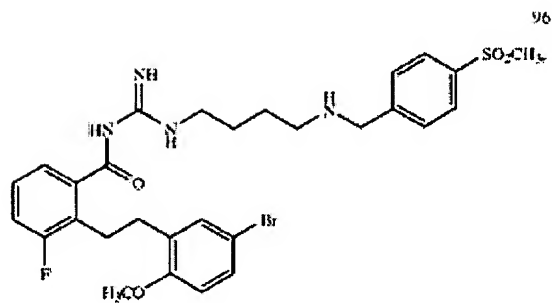
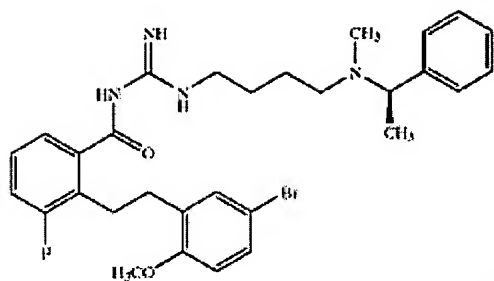


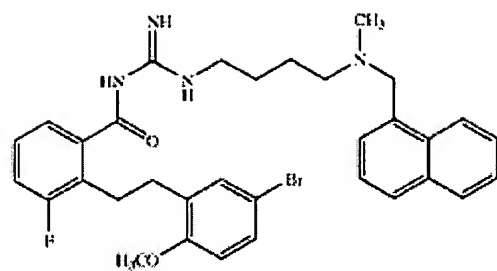




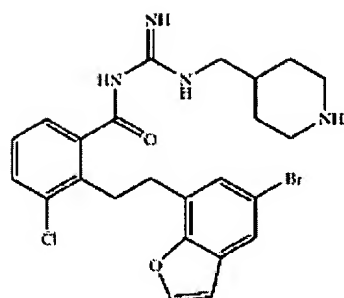




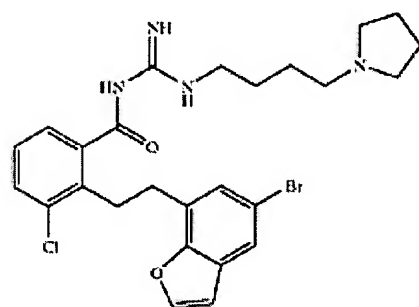




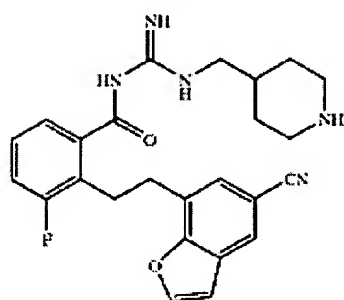
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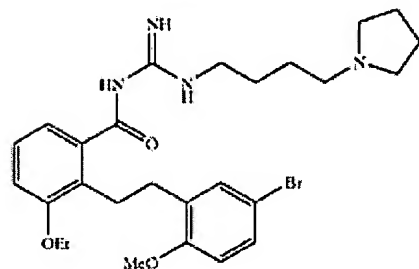
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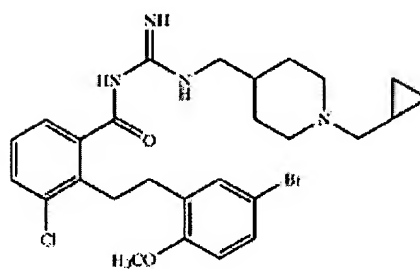
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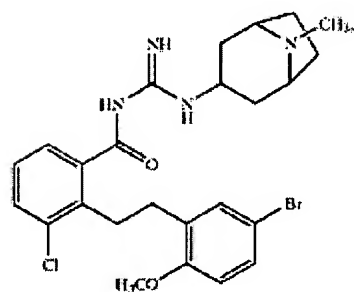
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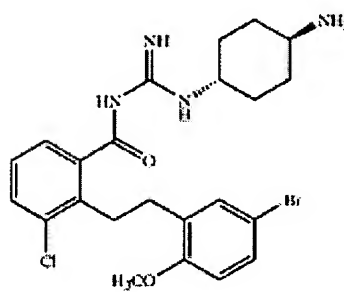
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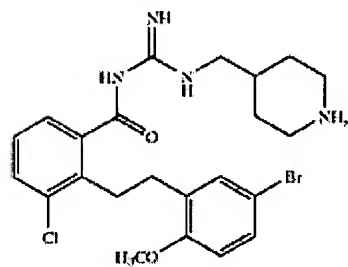
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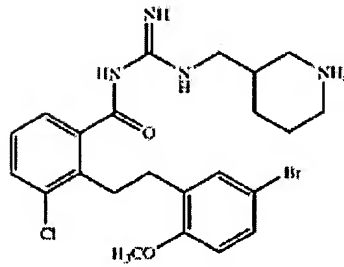
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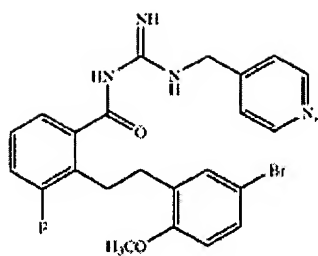
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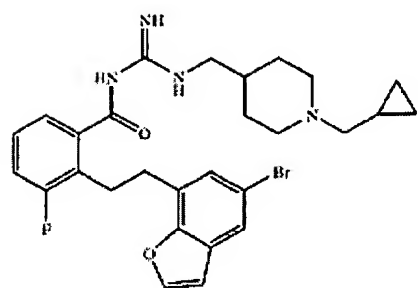
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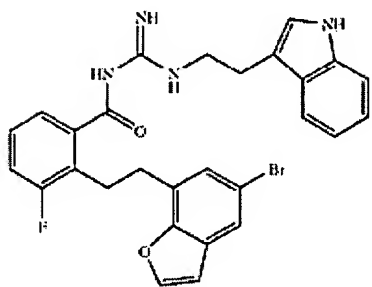
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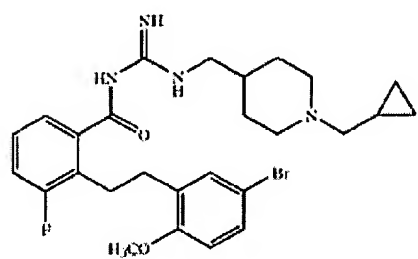
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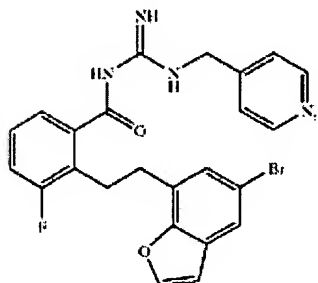
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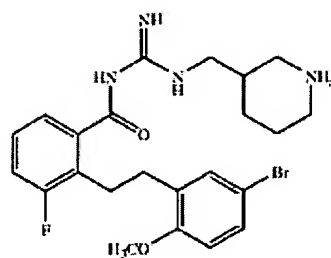
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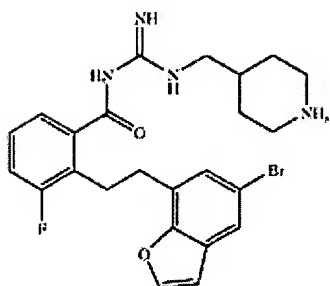
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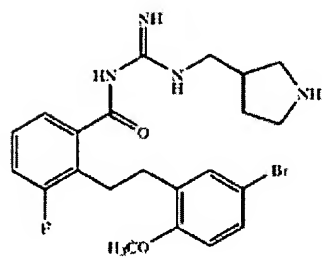
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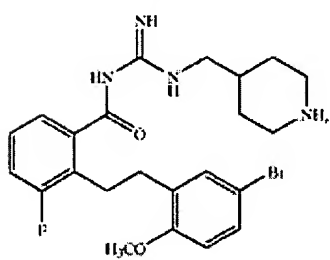
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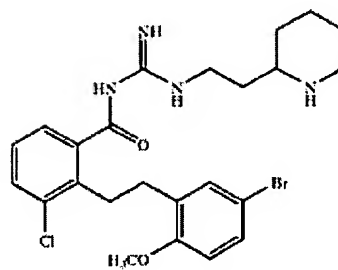
116



117

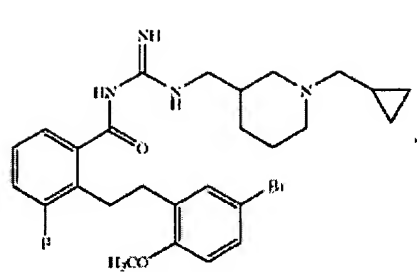


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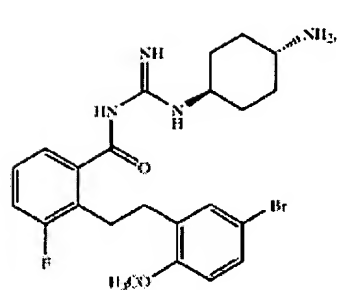


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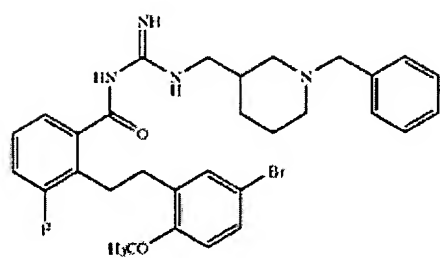




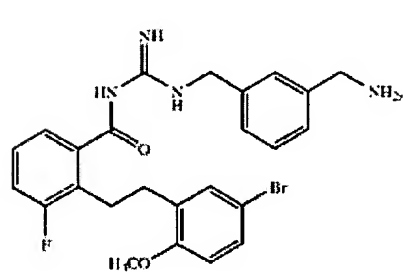
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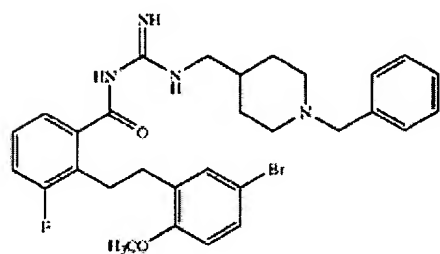
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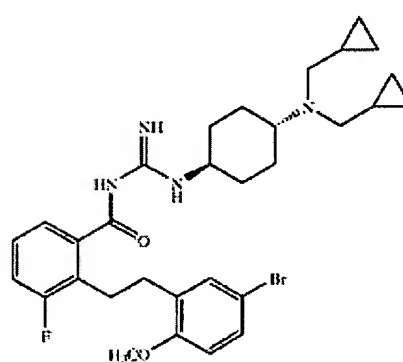
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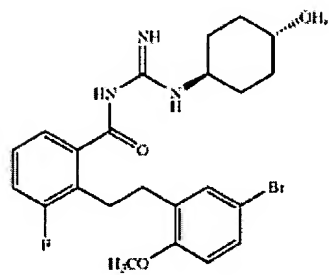
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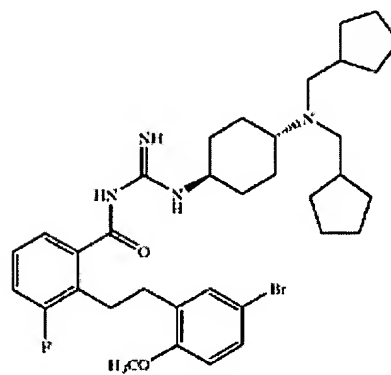
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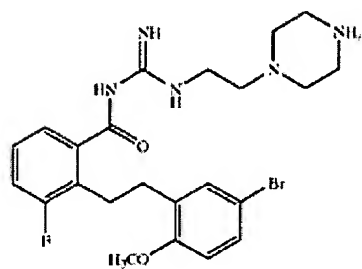
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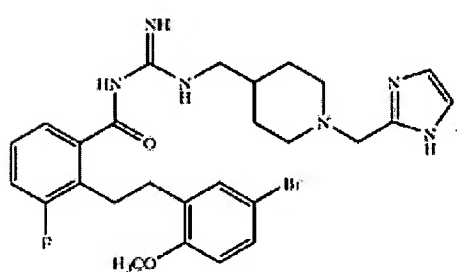
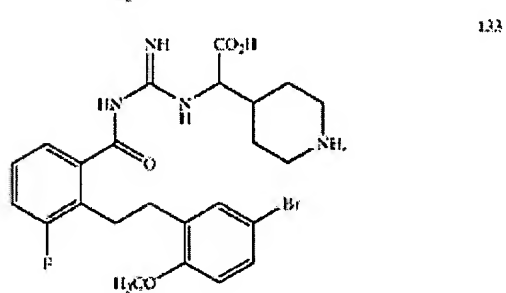
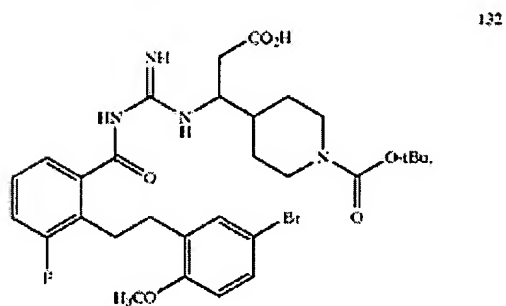
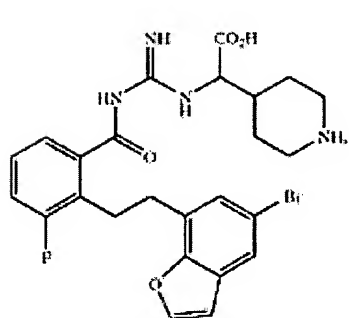
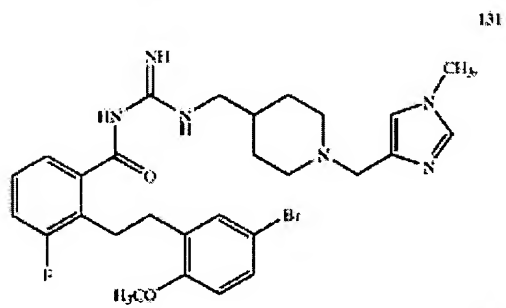
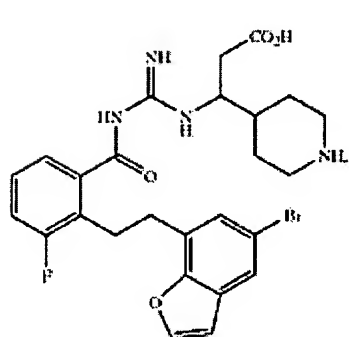
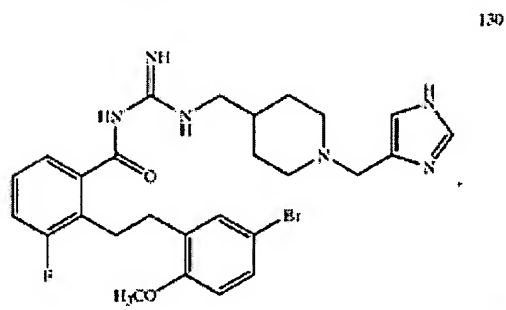
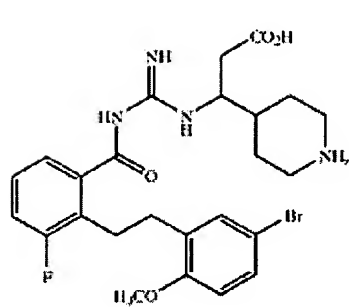
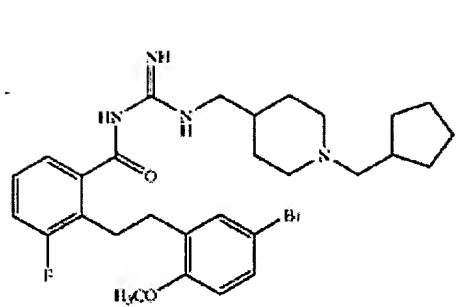
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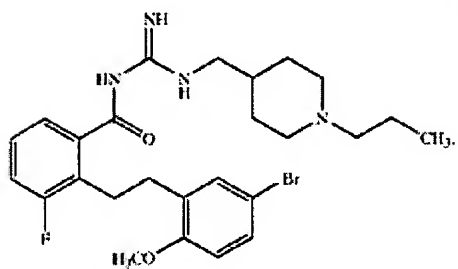
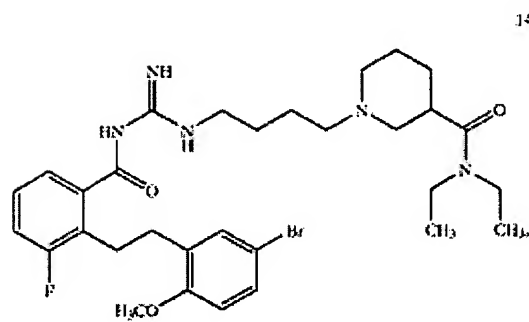
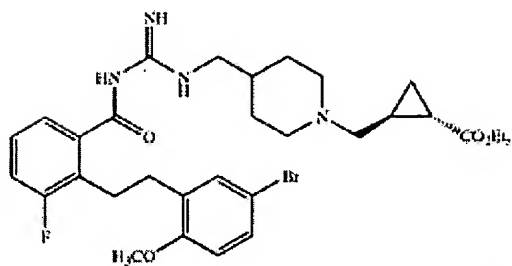
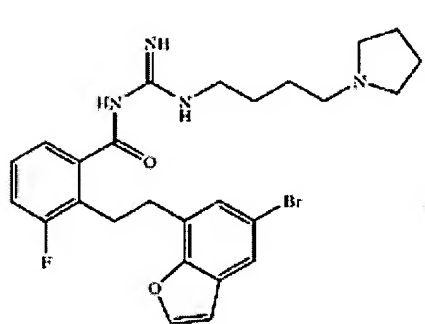
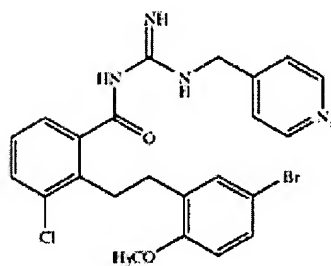
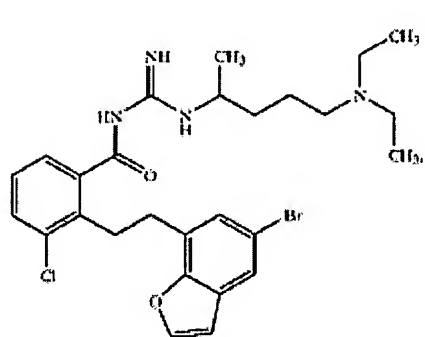
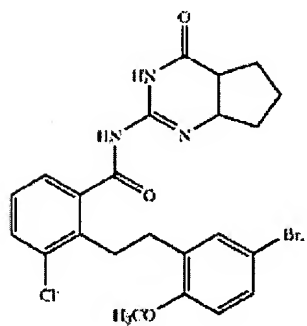
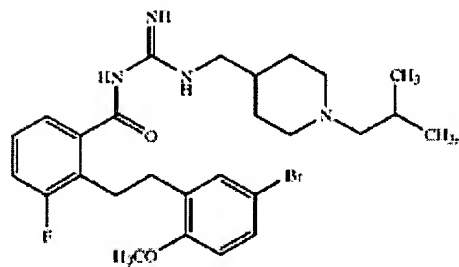
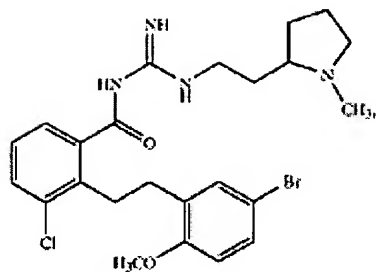


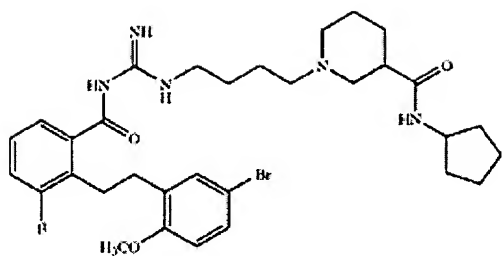
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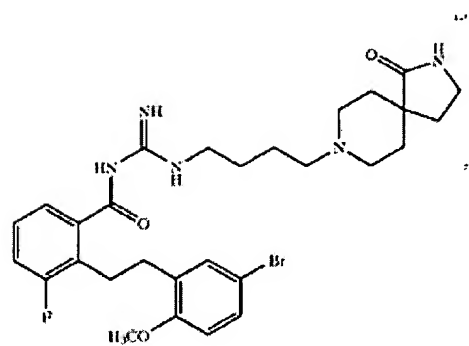
128



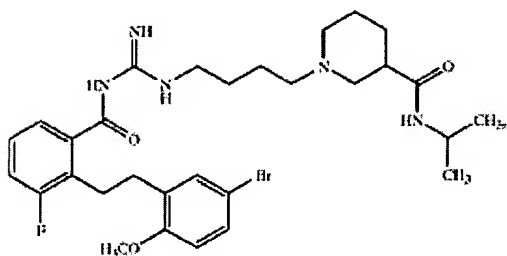




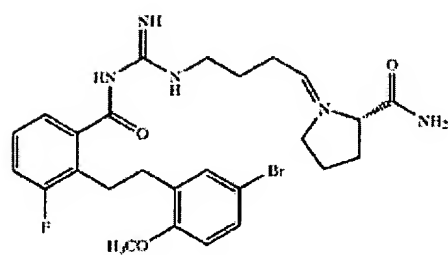
148



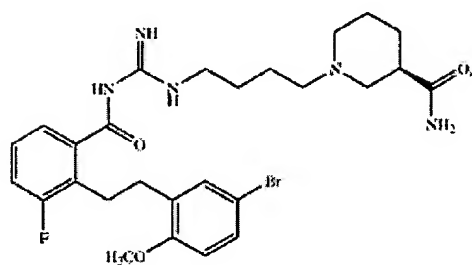
151



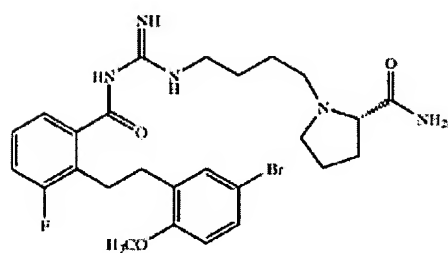
149



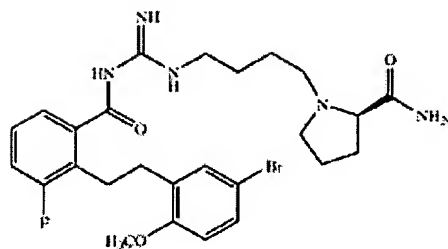
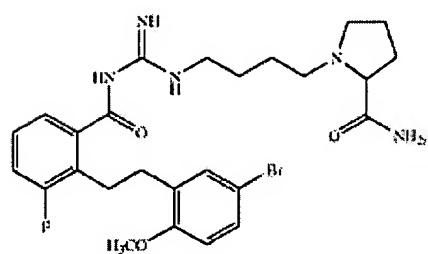
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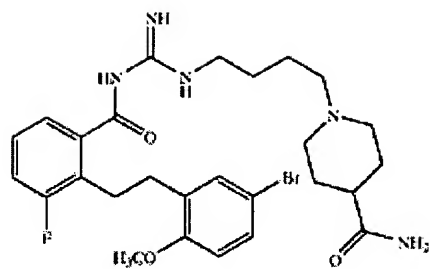


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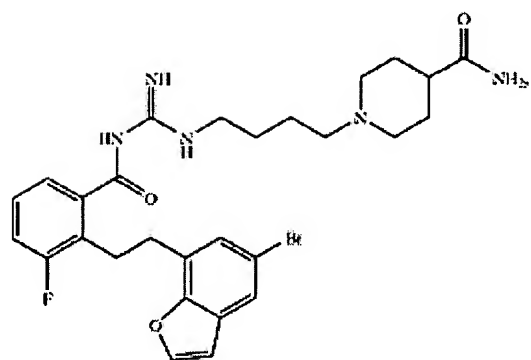


153

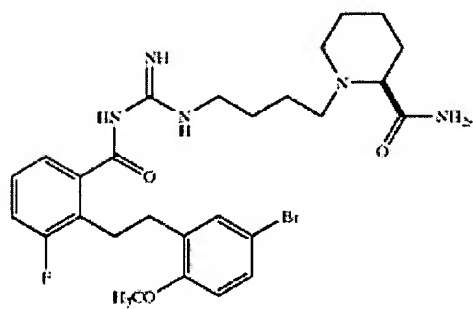




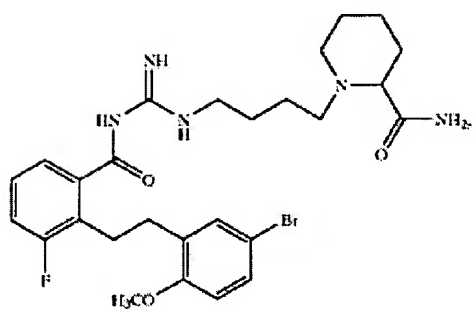
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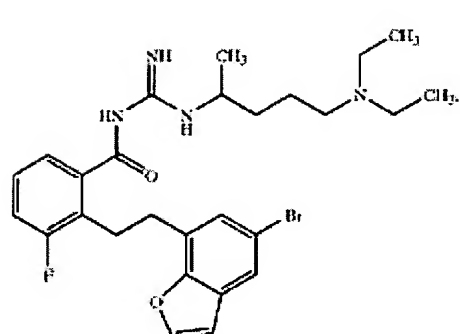
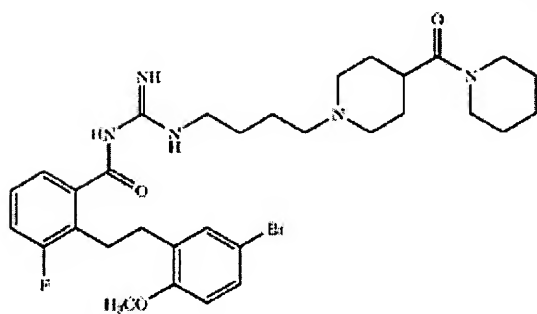
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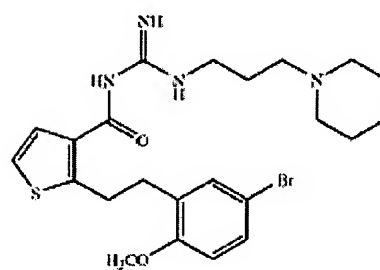
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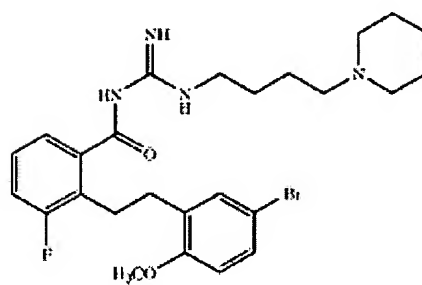
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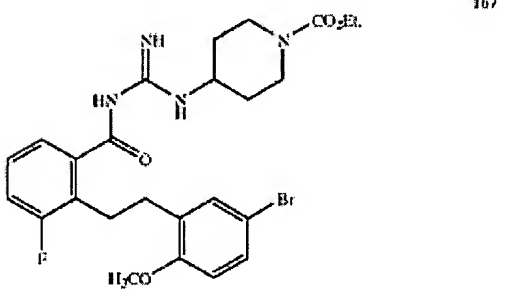
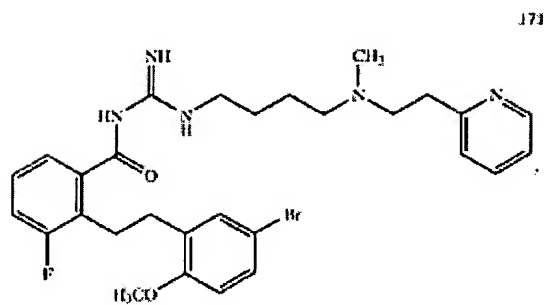
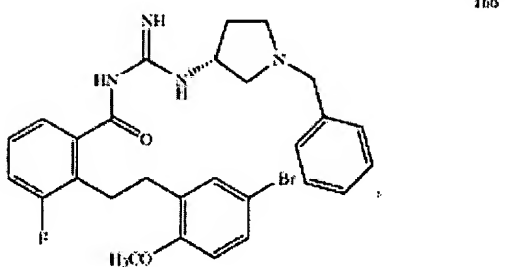
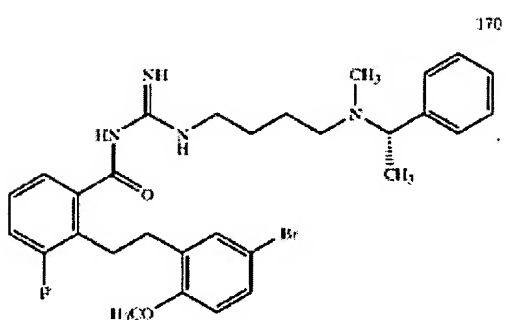
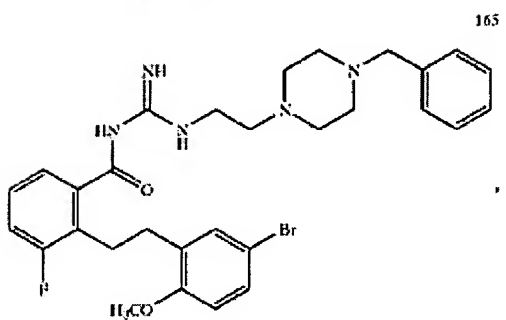
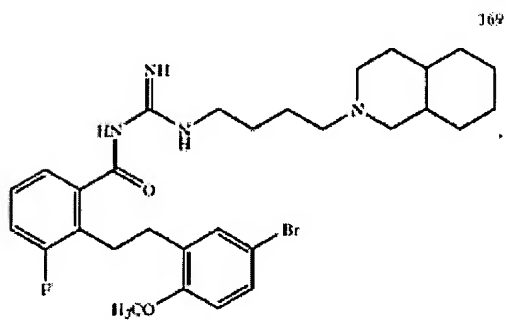
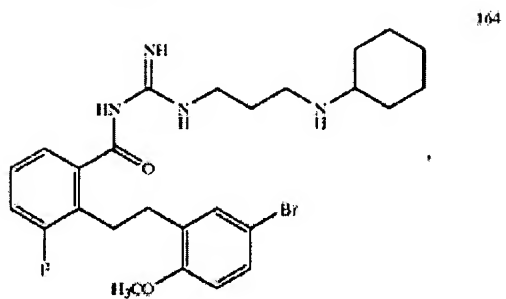
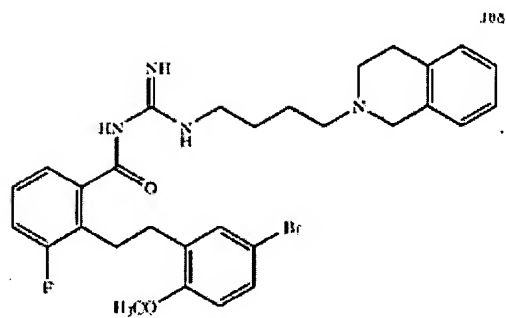
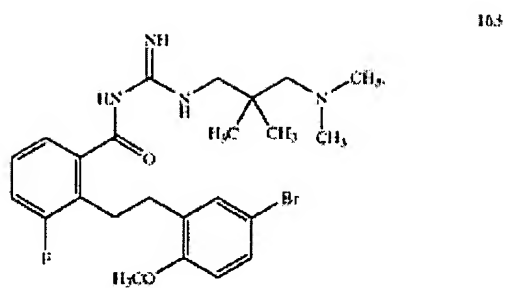
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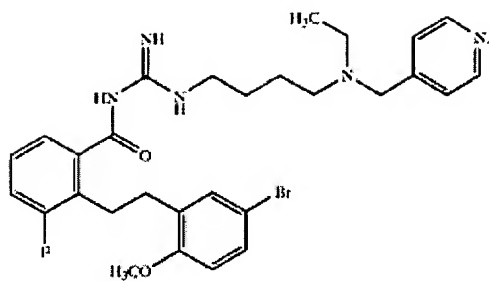
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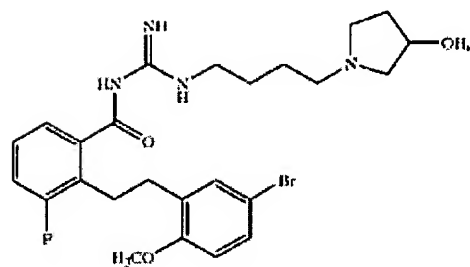
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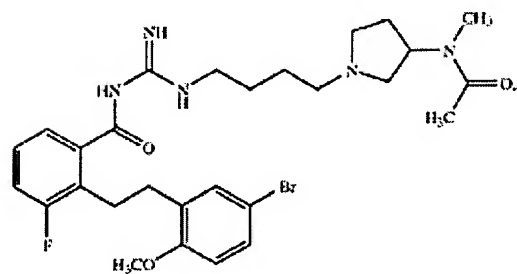
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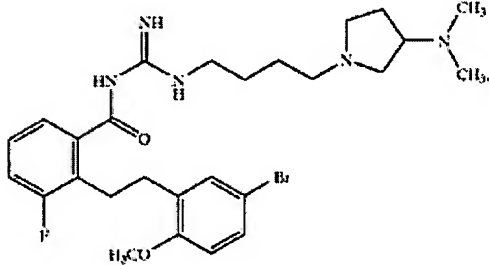
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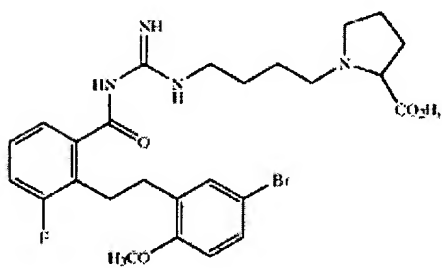
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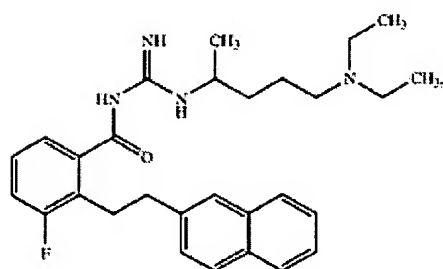
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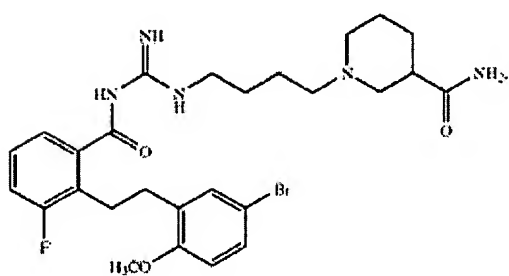
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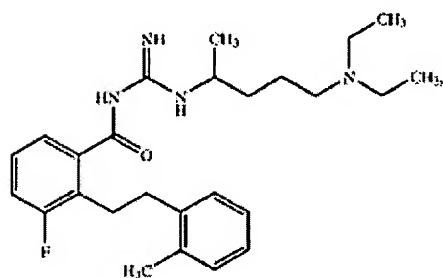
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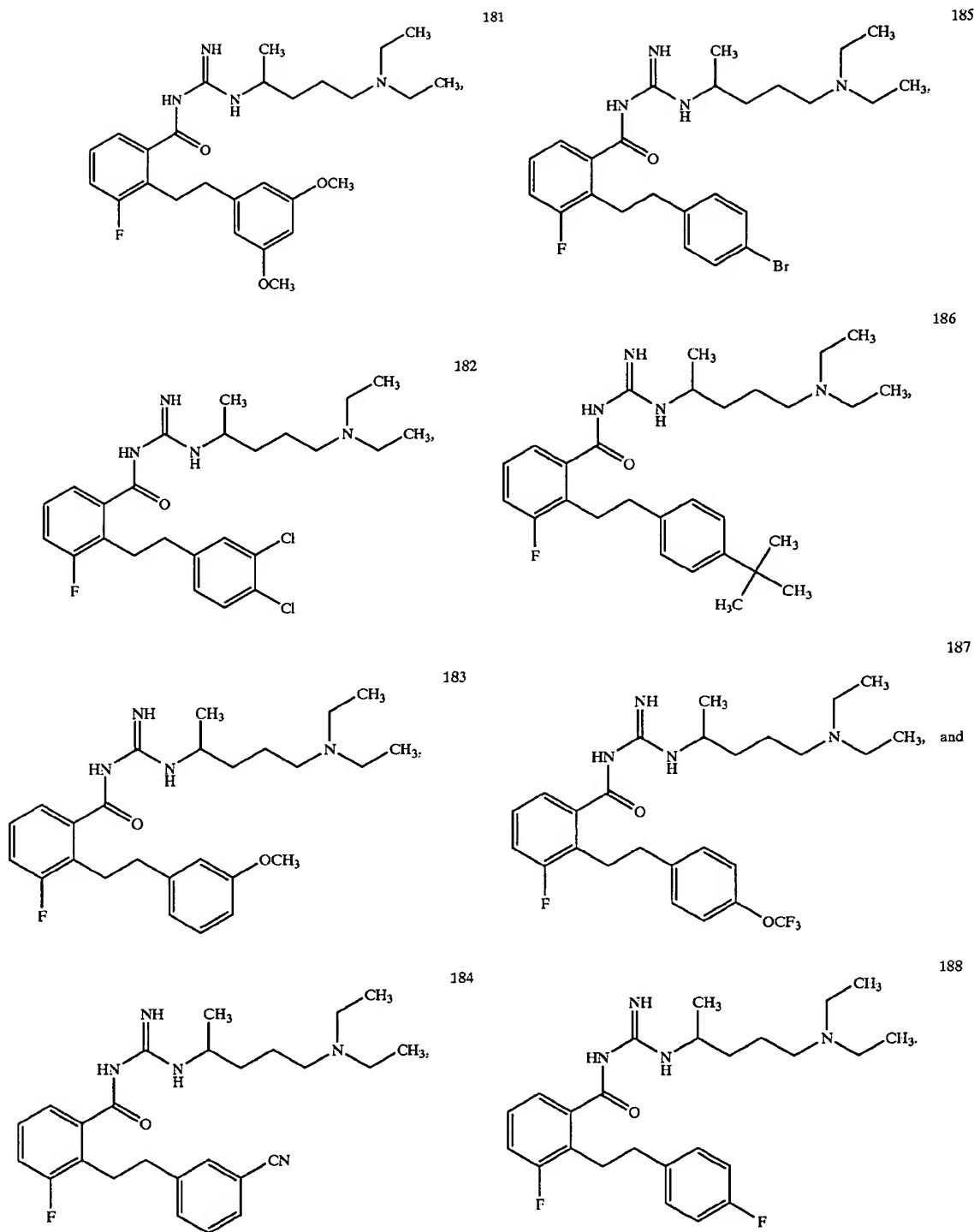


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Claim 22. (Original) A pharmaceutical composition comprising a compound according to claim 1 and a pharmaceutically acceptable carrier.

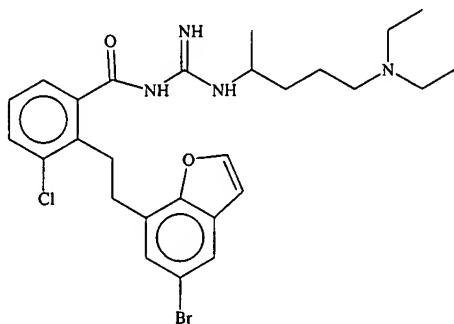


- Claim 23. (Withdrawn) A method of treating an MC4-R associated disorder in a patient in need thereof comprising administering to said patient a compound of formula (I) in claim 1.
- Claim 24. (Withdrawn) A method of treating an MC4-R associated disorder in a patient in need thereof comprising administering to said patient a pharmaceutical composition comprising a compound of formula (I) in claim 1.
- Claim 25. (Withdrawn) A method of treating a weight loss disorder in a subject identified as in need of such treatment comprising administering a compound of formula (I) in claim 1.
- Claim 26. (Withdrawn) The method of claim 25, wherein the weight loss disorder is a cachexia, aging involuntary weight loss, catabolic wasting, or anorexia.
- Claim 27. (Withdrawn) The method of claim 26, wherein cachexia is cancer cachexia, cardiac cachexia, chronic illness cachexia, or AIDS cachexia.
- Claim 28. (Withdrawn) A method of treating a bone associated disorder in a subject identified as in need of such treatment comprising administering a compound of formula (I) in claim 1.
- Claim 29. (Withdrawn) The method of claim 28, wherein the bone associated disorder is osteoporosis, bone fractures, bone formation associated with surgical procedures, osteogenesis imperfecta, hypophosphatasia, Paget's disease, fibrous dysplasia, osteopetrosis, myeloma bone disease, or the depletion of calcium in bone.
- Claim 30. (Withdrawn) A method of treating a pain disorder in a subject identified as in need of such treatment comprising administering a compound of formula (I) in claim 1.

Claim 31. (Withdrawn) The method of claim 30, wherein the neuronal disorder is neuropathic pain or allodynia.

**Claim 32. (Withdrawn)** A method of inhibiting MC4-R activity in a patient in need thereof comprising administering to said patient a pharmaceutical composition comprising a compound of formula (I) in claim 1.

**Claim 33. (New)**



or a salt thereof.

Claim 34. (New) A pharmaceutical composition comprising a compound according to claim 33 and a pharmaceutically acceptable carrier.

Claim 35. (New) A method of treating an MC4-R associated disorder in a patient in need thereof comprising administering to said patient a compound according to claim 33.